NATURE

No. 4058 SATURDAY, AUGUST 9, 1947 Vol. 160

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Telegrams : Phusis Lesquare London
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T. G. Scott & Son, Ltd., Talbot House, 9 Arundel Street, London, W.C.2
Telephone : Temple Bar 1942
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BRITISH COLONIAL DEVELOPMENT

THE announcement by Mr. Creech Jones in the House of Commons on June 25 of the Government's proposal to establish a Colonial Development Corporation marks a definite stage towards the establishment of a new Colonial system aimed at raising the standard of living in British Colonies, which has been implicit in such recent proposals as Dr. E. B. Worthington's Development Plan for Uganda, and the plan for the production of groundnuts in East Africa. The Ground-nut Corporation scheme is concerned primarily with foodstuffs; but its contribution to the raising of the standard of living in Tanganyika, Northern Rhodesia and Kenya may well far outshadow its contribution towards meeting the world shortage of fats. The twenty-five million pounds required for this Corporation is indeed to be provided separately; but it will none the less be as distinct a contribution to Colonial welfare as the capital of £100,000,000 of the Colonial Development Corporation now announced.

Mr. Creech Jones said that the Corporation would operate on commercial principles, and that its object would be to establish or assist any enterprise in the Colonies which is designed to increase their general productive capacity. While these enterprises might be mainly agricultural, the Corporation would be able to undertake any enterprise which served the general object either itself, or through subsidiary organisations for individual projects, or by assisting existing enterprises. Unlike the Development Board for the Colonies canvassed unofficially a few years ago, the new Corporation will be subordinate both to the Colonial Office and the Colonial Governments. The intention is that the Corporation and its subsidiaries should operate generally in close consultation with Colonial Governments, to ensure that their activities are conducted in the way best suited to promote the welfare of the Colonial peoples.

It was made clear that the Corporation is intended to supplement, not supplant, private enterprise. The Government would continue its policy of encouraging public utilities and other suitable forms of public enterprise; but it would also welcome private enterprise and investment so long as they are in harmony with the plans of Colonial Governments for social and economic development. Mr. Creech Jones, in reply to questions, indicated that the Government is alive to the importance of decentralization, and that although the head office must be in London, certain concerns and enterprises would have their principal offices in the territories with which they are strictly concerned.

The scheme as outlined by Mr. Creech Jones is thus based on the realization that capital on a far larger scale than is made available under the Colonial Development and Welfare Act is needed to raise the standard of living in the British Colonial Empire. What is equally important, there appears to be visualized co-operation with other Government departments besides the Colonial Office, such as the Board of Trade and the Ministry of Food. Several Departments are in fact already working together on

a survey of opportunities for new commodity production in the Colonial Empire. Success may largely depend on the extent to which there is stimulated on a much larger scale that two-way flow of ideas, already to be seen on a modest scale, resulting from the work of the Colonial Research Committee and the Colonial Products Research Council. It will certainly depend largely on the extent to which there is secured the co-operation of scientific workers in the way that is so conspicuously a feature both of the ground-nuts project for East Africa and the development plan advanced by Dr. E. B. Worthington for Uganda*. The feature of Dr. Worthington's plan is the suggestion that pilot development schemes should be used to try out ideas of land use and social services which later can be applied to large parts of the Protectorate. They should also be areas of intensive production, at first by State enterprise, in country which is at present largely undeveloped. In this way, Dr. Worthington contends, about twice as much expenditure on public services per head of population as is possible in the country as a whole will pay dividends after ten years.

Dr. Worthington recognizes and states the fundamental problem in Colonial development and welfare which the general schemes under the new Corporation will equally have to face. The average standard of living cannot rise and public services cannot expand unless production increases at a greater rate than population. Ten years, he suggests, should be devoted to a production drive while increasing social services at a rate greater than population increase. If success is achieved, Uganda will be able to support mass education and a mass health scheme during the following decennium.

In the production drive, the great asset of Uganda is not man-power but undeveloped land and water. The chief factors which limit development are the lack of fundamental formation about the country and the people; a system of production incompatible with the full use of natural resources; lack of capacity of the African for physical work; and power based on the most inefficient of fuels. Dr. Worthington's plan aims at solving the fundamental problem of balance between population and production by reducing these limiting factors, although he is doubtful whether adequate results can be achieved without some degree of compulsion, possibly the equivalent of that which is applied in Britain to-day.

The pilot schemes suggested are for the development of a self-contained piece of land, preferably a catchment area of say 500 square miles, sparsely inhabited on account of tsetse fly. Settlers up to 6,000 families would be employed for the first few years, while the whole area was being developed as a Government estate. At this stage there would be only six Europeans as against 42 Europeans to about 1,800 Africans in the resident units of the ground-nut scheme. Later, most of the settlers would become tenant farmers under close supervision, a part of the unit being retained as a Government farm. Initial clearing and subsequent cultivation would be undertaken with mechanical assistance, where possible. Communications, forestry, water-control, agriculture, fisheries and social services would be organised for the efficient development of land, water and people, with an emphasis on productive services.

The scheme is finely conceived and represents a scientific approach that might well be adopted more widely. It is not only in research in applied biology, in animal husbandry, forestry, fisheries, hydrology, meteorology, agriculture and the like that science can contribute so much to Colonial development and welfare. It is becoming more and more clear that the scientific approach is the only one that holds out real hope of a solution to the all-important human problem. Although Dr. Worthington makes like reference to the contribution of the social sciences, his scheme, like the ground-nut scheme, is in keeping with the idea that Mr. Aldous Huxley outlines in his recent book, "Science, Liberty and Peace"*, of developing regional self-sufficiency as a decentralizing and stabilizing factor in world order. It is equally in line with ideas which Col. W. R. Crocker emphasizes in his penetrating commentary†, "On Governing Colonies", of concentrating less on what is ideal from the European point of view and more on what is practical from that of the African, on the preventive rather than the remedial aspect of public health and the essential idea of the Tennessee Valley Authority, in which the association of the ordinary people affected by the scheme is first secured. Similar ideas are stressed by Sir J. Hawthorn Hall, the Governor of Uganda, in some notes on the economic development of Uganda which preface Dr. Worthington's report.

That the regional aspect is present in the mind of the Colonial Secretary is shown by his recent comments on the eighteen months work of the Colonial Economic and Development Council. Nearly all the thirty-five territories concerned have submitted ten-year development plans, although some plans have been referred back with comments or suggestions. But Mr. Creech Jones has stressed the importance of regional planning and development in contiguous Colonial territories such as East, Central and West Africa, and also in the West Indies. In a memorandum accompanying his dispatch of February 14, 1947, on closer association of the British West Indian Colonies, he refers to the manifest need in all the Colonies concerned for improved facilities for research, including surveys and statistical services, in order that plans for economic development and social welfare may be soundly conceived and wisely executed. Except in co-operation, the Colonies will not generally be able to afford or fully to employ the services of the experts required to fulfil those functions. It was announced in this dispatch (Cmd. 7120. H.M. Stationery Office, May 1947. 9*d*. net) that a conference is to be held at Montego Bay, Jamaica, in September, and its outcome will be watched with great interest by all who are aware of the potentialities which have already been revealed in the Caribbean.

* Uganda Protectorate. A Development for Uganda. By Dr. E. B. Worthington. Pp. xii+112. (Entebbe: Government Press, 1946.) 2*s*. 6*d*.

* Science, Liberty and Peace. By Aldous Huxley. Pp. 64. (London: Chapman and Hall, 1947.) 3*s*. 6*d*. net.

† On Governing Colonies. By W. R. Crocker. Pp. 152. (London: Allen and Unwin, 1947.) 10*s*. 6*d*. net.

There are other aspects of the man-power situation which are of fundamental importance in all these proposals. Inevitably the formation of a Colonial Development Corporation, like the Ground-nut Corporation, with its various subsidiary schemes and ramifications, tends to widen the range of opportunities which the Colonial Service offers and to call for more varied abilities among the members of that service. No thoughtful reader of Col. Crocker's recent comparative study of British, French, Belgian and other Colonial practice and experience can doubt the need for recruits of high quality to the Colonial Service, the great scope for initiative and responsibility which that service offers, or the need for a new outlook in some quarters and for drastic changes in organisation, practice and the transfer and promotion of staff. Ultimately, it is on the quality of the staff by which the Development and Welfare Schemes are administered, their vision and understanding of the needs and minds of the native peoples, their appreciation of the contribution of science, of the problems and opportunities of the private and public corporations seeking to serve the needs of the native peoples and of the world, that success will depend. Nor will the ablest men and women be forthcoming and their zeal and enthusiasm maintained unimpaired unless the conditions of service are such as to call forth their best efforts and to give them the continued stimulus and incentive that will spring from manifest participation in the high task not merely of serving the material and social needs of the Colonial peoples, but even more of training, inspiring and guiding their future leaders in accordance with those new conceptions of imperial responsibility which mark the third Colonial Empire now developing. It should be a first pre-occupation of the Government to see that no timidities or inhibitions of Colonial administration are allowed to hinder the full use of all the expert knowledge of Colonial resources and methods of treatment that have been accumulating in the last four years, or the vigorous prosecution of the fresh researches still required. Above all, nothing must be allowed to frustrate the boldness of imagination with which these new opportunities must be served.

CHEMICAL CRYSTALLOGRAPHY

Chemical Crystallography

An Introduction to Optical and X-ray Methods. By C. W. Bunn. Pp. xii+422+13 plates. (Oxford: Clarendon Press; London: Oxford University Press, 1945.) 25*s*. net.

PROF. VICTOR GOLDSCHMIDT used to say that, over the door of his laboratory in Heidelberg, he would like to have written "Die Kristallographie ist die Königin des Wissenschaften"; and while he said this chiefly because he personally was fascinated by the external shapes of crystals and their formal geometry, he may perhaps also have thought of crystallography as holding a distinctive place among the sciences, at once isolated and yet pervading. Indeed, crystallography as we know it to-day is in many ways a curious subject. It has come to be principally concerned with the use of X-ray diffraction effects to study, to varying degrees of precision, the arrangement of the atoms in substances, many of which can scarcely be called crystalline at all. The techniques employed belong largely to mathematics and physics, and the information derived is of fundamental importance to subjects so far apart as metallurgy and biology, and particularly to chemistry. There seems, perhaps, something unsatisfactory in the way we cling to so precise a term as 'crystallography' to cover all these developments. Yet, as the combined international body of 'crystallographers' discovered in recent discussions, it is difficult to find any other term to which we can give all the meanings we associate now with the word 'crystallography'.

There is more than one reason for this situation. Without the early classification of the geometrical form of crystals and the mathematical developments of space-group theory, the problem of structure analysis by physical methods is at least much more difficult. Far more of the kind of exact data on which most interest centres—the details of the arrangement of atoms in space and the exact distances between them—can be got once a really crystalline substance is available (some justification for all the hours that have been spent in chemical research in the preparation of 'a crystalline derivative'). But the apparently complex background of knowledge, mathematical, physical and crystallographic, which is required for the proper use of X-ray analysis, makes the subject too often seem too difficult just to those who should find its applications most useful, and particularly to students and research workers in chemistry.

It is the great merit of Mr. Bunn's book that it does very largely attempt to develop a new approach to the study of crystallographic methods based on the use in chemical research of a variety of ways of observing crystals and their structure, both new and old. This new approach is extremely practical. It is designed to meet the needs of those who wish to know, in the first place, what types of chemical information can be gained by using crystallographic methods, and secondly, the essential practical and theoretical details necessary for operating these methods. The relations between these different aspects of the subject are outlined in a very clear general survey of the field which forms the opening section of his "Chemical Crystallography". This survey indicates the limitations as well as the applications of X-ray methods; it also describes the general division of the subject-matter of the book into different, more specialized sections.

The primary purpose in chemical research of getting a 'crystalline derivative' is usually for the identification of different chemical individuals. The assistance which can be given in this direction by crystallographic techniques, particularly crystal morphology and optics and X-ray powder photographs, forms the subject of the first major division of the book. Around this theme is developed the necessary formal information on the types of crystal symmetry possible, on the examination of optic figures and the measurement of refractive indices, and also elementary theory of X-ray diffraction. Here there are important contributions to the presentation of the subject as a whole. For example, the indexing of crystal faces is notoriously difficult for the non-specialist to appreciate. Mr. Bunn begins by showing excellent photographs of crystals growing, and leads by easy stages through the relation of the observed crystal layers to the packing of atoms in space, and so to a

derivation of indices for the crystal faces which seems both natural and simple. Further, this derivation presents the indexing process in a way which is very helpful in the later consideration of X-ray analysis.

The second part of the book is devoted to structure determination. It covers both the experimental methods of X-ray photography, the indexing of the more important varieties of photographs, and the actual processes of deduction of the atomic positions from the experimental observations. The methods are illustrated by a section which gives a variety of examples of actual structure determinations carried out both on inorganic and organic substances, and also on certain types of imperfectly crystalline material, for example, long-chain polymers. The use of Fourier series, both in the determination and refinement of structures, is (rather briefly) described. Crystallography is, like all good sciences, also an art, and the methods of practising it differ in the hands of different investigators. One realizes in the course of these chapters not only the variety of the problems of structure analysis, but also something of Mr. Bunn's own position as a successful 'artist' with his own particular approach to these general problems. His own technical contributions in this field are already having considerable effect on the general strategy of X-ray analysis, particularly his practical development of Bragg's optical diffraction method, which is here for the first time fully described. The section concludes on quite different topics, the bearing of crystallographic research on what has been termed the 'texture' of materials, the calculation of particle size from broadening of X-ray lines, and the determination of strain.

I suppose it would be impossible for any book to cover so wide a field as this in a new and individual way without leaving openings for criticism. It seems rather unnatural, for example, to describe powder photography before single-crystal photography. Certain sections seem really too short for maximum usefulness; for example, that on crystal structure and physical properties. There are also a few misprints in the book (for example, the formula on p. 158), and one section at least, that on rhombohedral lattices, p. 135, which is quite misleading. But almost immediately, arguments arise in defence at least of Mr. Bunn's general treatment. There are definite practical advantages in the association of powder photography with other methods of crystal identification; and any great lengthening of an individual section would certainly detract from the usefulness of the book as a readable and coherent survey of the field as a whole. The serious student of the subject has, sooner or later, to turn to original papers, and for this purpose excellent references are supplied.

Taken all together, this book is most welcome. It is very clear and easy to understand, and also beautifully and plentifully illustrated. It has already proved its value in crystallographic teaching and practice, and should play an important part in the development of the subject as one of the established tools of chemical research in the widest sense. But while Bunn's "Chemical Crystallography" is certainly a book that has been badly needed, it may perhaps be fair to add that it is not the only badly needed book on the subject of crystallography to-day. Many of the chapters here could usefully be enlarged into monographs or even text-books. It is to be hoped that some at least of these books are in process of construction.

D. CROWFOOT

EXPANSIONS IN EIGENFUNCTIONS

Eigenfunction Expansions associated with Second-Order Differential Equations

By Prof. E. C. Titchmarsh. Pp. vii + 176. (Oxford: Clarendon Press; London: Oxford University Press, 1946.) 20*s.* net.

THE subject of Prof. Titchmarsh's book is the expansion of an arbitrary function in terms of the eigenfunctions of linear differential equations; to be precise, in terms of functions which satisfy an equation of the form

$$\frac{d^2y}{dx^2} - q(x)y + \lambda y = 0. \qquad (1)$$

Problems of this nature arise in the theory of vibrations of elastic media, where we wish to express an arbitrary vibration in terms of the stationary vibrations: here the corresponding equations are the classical Sturm–Liouville equations. During this century, similar problems have become important in connexion with the Schrödinger equation of quantum mechanics; the physical problem corresponding to the mathematical problem of the expansion of an arbitrary function is the expression of an arbitrary state of a system in terms of the eigenstates of an observable. The corresponding differential equations are of singular type; that is, the interval involved is infinite, or the function $q(x)$ becomes infinite at the ends of the interval.

Prof. Titchmarsh has devoted most of his attention to the singular case for an infinite interval. The ordinary Sturm–Liouville problem is dealt with briefly in one of the early chapters. The rest of the book is devoted mainly to the consideration of the nature of the spectrum, that is, roughly speaking, of the set of values of λ for which the equation (1) has solutions, and to the convergence of the resulting expansions for arbitrary functions. In many cases the spectrum consists of isolated points, and the resulting expansion is a series similar to a Fourier series; in other cases the spectrum consists of all the points of an interval and the expansion is an integral, similar to a Fourier integral; in other cases, of which the Schrödinger equation for a hydrogen atom is a notable example, there is a combination of both types. A very interesting chapter shows how these different cases result from different types of behaviour of $q(x)$ as x tends to infinity.

Another important problem is the distribution of the eigenvalues, or of the size of the n^{th} eigenvalue when the eigenvalues are arranged in order of magnitude. Results are given for this in which the semi-intuitive arguments of physicists are replaced by rigorous analysis.

The greater part of the book is devoted to the convergence or summability of the expansions. These have in the past been treated in the general case almost exclusively from the point of view of convergence in mean square, and results for ordinary convergence or summability at a point have been obtained in the main only for particular cases. Prof. Titchmarsh gives results for the convergence of these expansions when the function $q(x)$ obeys certain sets of conditions which hold in the important particular cases; and he shows that under wider conditions the series expansion is summable to the function represented: this function must obey the same conditions as are necessary for the convergence or summability of a Fourier series.

In the past these problems have been treated either on the basis of the theory of integral equations or the theory of linear operators in Hilbert space. Prof. Titchmarsh has used the theory of functions of a complex variable, and makes no appeal to the methods mentioned. His method is to express the solution of the equation as a contour integral and then to get his results directly by the powerful methods of contour integration. The earlier treatments are perhaps more suitable for a discussion of mean square convergence, or for unifying the theory with that of integral equations and other linear operators, but are certainly more difficult to apply to the study of the problems here treated.

The book has the lucidity and mastery of analytical method which characterize the author's well-known books on the "Theory of Functions" and "Fourier Integrals"; but unlike these it gives not an exposition *ab initio* of the subject as a whole but only of results and methods for the problems mentioned above, which were very largely developed by Prof. Titchmarsh in his recent papers on the subject. It does not attempt an account of the physical background of the subject. All the important special cases are dealt with as examples, but without detailed accounts of the special functions involved which are dealt with in the standard treatises on differential equations. However, a reader with a knowledge of complex variable theory should be able to follow the analysis. As a whole, the book is an important contribution to analysis, and should prove of interest to mathematical physicists as well as to mathematicians.

NAMES INTO CIPHER

A New Notation and Enumeration System for Organic Compounds

By Dr. G. Malcolm Dyson. Pp. iv + 63. (London, New York and Toronto: Longmans, Green and Co., Ltd., 1947.) 7*s*. 6*d*. net.

WHAT Dr. Dyson has given us in this volume is less a book on nomenclature than a 'blueprint' or a code manual for the professional indexer. Although the system of notation which he describes demands, and indeed merits, careful scrutiny and examination by organic chemists who are specialists in different fields, it can scarcely be regarded as a contribution to the problem of organic chemical nomenclature properly understood, and the ordinary organic chemist will find what he requires in Dr. Dyson's original lecture last October as since published by the Royal Institute of Chemistry rather than in the present book. The major part of the book is devoted to a careful and detailed exposition of Dr. Dyson's system of ciphering, in which the basic carbon skeleton is first ciphered by a linear series of letters and numerals, with the assistance of commas, stops and semi-colons. All fused-ring systems are enumerated in terms of six conventional ring systems. The functional groups are then similarly ciphered, and the system is logical as well as ingenious and concise. Dr. Dyson claims, moreover, that it has the advantage that there is only one possible cipher for any one chemical compound.

That is an impressive claim, and has to be weighed carefully against any doubts one might entertain as to the unfailing accuracy with which the ordinary organic chemist would apply the rules in practice; and equally, his unerring eye not merely for departures from the logical application of the rules but also for mechanical errors in the transcription of the cipher. An error in nomenclature is usually self-evident to an expert in a particular field, but this is scarcely true to the same extent of a cipher or indeed of a number; and that is probably one reason why the Universal Decimal Classification is unlikely ever to be adopted as a working tool in the indexing of organic chemical compounds.

Dr. Dyson appears, in fact, to have dismissed this question of nomenclature too summarily, and what he has to say under this head is much better put in his original lecture. He does not here show sufficient apprehension of the purposes of nomenclature, or of those relations between its users which are responsible alike for the introduction of trivial names and for departures from systems. Granting that such names as 'coronene', 'phthalazine', or 'rubicene' have been coined because there are no satisfactory systematic alternatives, regarded as symbols, for certain purposes, they may prove as satisfactory as the ciphers suggested by Dr. Dyson. It must be remembered that in particular fields, such as dyestuffs, or synthetic resins or other plastics, the organic chemist will think in the units of which the structure is built up: no dyestuff chemist would attempt to use the systematic name for dianisidine blue, any more than the plastics chemist would trouble with a systematic name for nylon. The trivial or systematic names of the substances brought together in practice in these complex molecules serve the needs of the chemist, even when he is accustomed to use the punched card technique as a regular tool.

The point has been elaborated because the future of the Dyson notation, once its logic and adequacy have been approved in a representative range of special fields, appears to depend on the use to which it is likely to be put. For the reason just given, its adoption by the industrial chemist is unlikely; and when we turn to consider its potentialities in regard to the production of a new lexicon of organic chemistry, a new 'Beilstein', or international indexing and abstracting, it should also be remembered that the present situation is unsatisfactory not only through confusion between different systems of nomenclature and failure to agree, but also for financial reasons. Empirical formulæ, for example, apart from the possible use of the Universal Decimal Classification, already provide a basis for such production if the necessary financial means to the end were willed. That financial aspect needs to be much more carefully examined before any decision is reached, or we may be in danger of finding that Dr. Dyson has prescribed a sledge-hammer to crush a nut.

Despite the ingenuity and logic of Dr. Dyson's notation, in this volume he appears to have missed an opportunity. He should have dealt much more persuasively with established systems of nomenclature, as he did in his original lecture, before proceeding to detail the new notation. A little more trouble in exposition of these systems and of present tendencies would have assisted him considerably to gain acceptance for his idea that a cipher rather than a systematic name is the best means for reference, classification and indexing. Finally, it might be observed that in production the volume compares badly with the lecture issued by the Royal Institute of Chemistry. Neither paper nor print are up to that standard, and to issue unbound at this price a volume which obviously demands close study and constant use is a serious defect.

R. BRIGHTMAN

WATER SUPPLY AND BIOLOGY*

By Prof. W. H. PEARSALL, F.R.S.
University College, London

WATER supply undertakings are primarily concerned with the production of an adequate supply of water of purity suitable for human and industrial consumption. Three features require attention. For human consumption it is of prime importance that the water must be free from deleterious substances and from disease-causing organisms. Secondly, for any purpose, uniformity of quality is a great virtue, and the quality must be such as to include freedom from unpleasant tastes or smells as well as from the more noticeable forms of chemical contamination. (We may leave on one side the question of the suitability of certain types of water for particular industrial uses.) Thirdly, the volume of water required is becoming an increasingly important factor in the problems of supply.

Great Britain has long enjoyed the provision of an admirable water supply. This is now taken for granted, and its advantages are so rarely realized that little credit is given to those responsible. We owe it primarily to the labours of the Rivers Pollution Commission in the 1850's and 60's.

The problem at that time was associated with a series of epidemics of typhoid fever and dysentery. It had been recognized that these were probably water-borne diseases, although due to germs which were excreted in human fæces. All water supplies which could be contaminated by human or animal excretions might thus be suspect, and the Rivers Pollution Commission was called on to investigate the matter and to survey the water resources of the country from this point of view.

They tackled the problem mainly by chemical methods, making use of the fact that animal organic matter is rich in nitrogen, a feature in which it contrasts markedly with plant materials. Thus in the former case the organic C/organic N ratio is low—and this is, in practice, coupled with a high rate of transformation of the material by bacteria to oxidized and inorganic forms of nitrogen-like nitrates. Two chemical features thus make a water suspicious from this point of view—a high nitrogen content and the presence of organic matter with a low C/N ratio.

I mention these activities of the Rivers Pollution Committee because their appreciations and methods were far in advance of their time, and 60–70 years were to elapse before it was generally realized that their technique for describing the origin and breakdown of organic matter was a fundamental one.

The attack on the problem of contamination by fæcal matter led also to the recognition of the fact that almost all surface waters were potentially dangerous. No better illustration of this fact can be given than what happened in Glasgow. There, in 1859, a public water supply from Loch Katrine replaced the numerous shallow wells that had formerly been used. Prior to 1859 a series of three typhoid epidemics had each resulted in the loss of more than two thousand lives. In epidemics, after that date, the number of lives lost fell to about one hundredth of the former number, and in all cases the infection was found to be associated with the continued use of the original supply from shallow wells.

*From a Chadwick Public Lecture delivered in the Chelsea Physic Garden on June 19.

The chemical methods formerly used for determining the character of water supplies have gradually been supplemented and largely replaced by biological methods. These make use of the fact that animal excreta constantly contain certain bacteria which survive for a time in water; but are unable to multiply materially under natural conditions. Particularly useful in this respect are forms like *Bact. coli.* and *B. welchii*. Thus use is now made of the presence or absence of such organisms under prescribed trial conditions to test for the freedom of the water examined from possibly dangerous contamination. To these testing methods have been added the use of bactericidal treatments, which have reduced the dangers from water-borne disease bacteria to vanishing point. Under modern conditions even isolated cases of typhoid fever or of other water-borne diseases are almost unknown, and they cause great consternation when they occur, as in the case of the Croydon epidemic just before the War. The freedom from such epidemics is due to the efficient methods of treatment and bacteriological control now employed.

The most recent developments in water supply problems are also associated with biological matters. Many of the difficulties in the way of efficient water-supply result from the large volumes required. These have risen steadily not only owing to improved methods and standards of sanitation but also to the development of industrial processes with a high water requirement. The aggregation of population in industrial Britain has greatly exaggerated the tendency, and it is becoming increasingly difficult to envisage the continuation of the present conditions without some system of overall planning, for all the larger centres of population must import water from a distance.

It is not, perhaps, generally realized that, in many rural areas also, existing population nearly or quite suffice to use all available supplies. In some areas, Derbyshire for example, no further increase in the rural population is possible. The difficulties in the way of obtaining adequate volumes of water have various effects. In southern England it has long been necessary to use river waters always more or less contaminated by sewage and by manurial treatments on the agricultural country through which they flow. It is only possible to use these waters safely because of the great improvements in bactericidal treatment and control now available.

The maximum amount of water available in any one place is the difference between the amount falling as rain and that evaporated back to the air. It is usually equivalent to about 10–12 inches of rain per annum in southern England. Rainfall is seasonal, so that it must be stored until required in the summer. The storage can be natural, underground stores as in the case of porous rock strata like chalk or limestone. The alternative is to utilize impounding reservoirs, and because these offer a habitat for plants and animals to grow in, many of the biological problems of water supply centre around the control of impounding reservoirs.

The organisms that appear may impart unsuitable quality or unpleasant tastes and smells to the water; but even if they do not, their presence necessitates filtration, and the quantities that at times must be removed add greatly to the difficulties of the water engineer. The algæ are the principal offenders in this respect, particularly diatoms and blue-green algæ. Some indication of the magnitude that the

problems of filtration may assume may be gleaned by the following example, illustrative particularly of conditions near London. A reservoir receiving water from the Thames and containing about 7 thousand million gallons might contain at times 110 tons of a single alga, *Fragilaria crotonensis*, measured as dry matter, and roughly a thousand tons as live algæ. From the volume of water normally filtered this involves a daily removal of at least a ton of dry weight, roughly equivalent to at least 10 tons of living alga.

It will be realized, then, that during periods of abundant algal growth, the algæ alone greatly complicate the problems of a waterworks engineer, for rapid replacement of filters becomes essential. Similar problems are sometimes presented by other aquatic organisms, notably the Cladocera or water fleas. However, the algæ and other aquatic plants have an especially important role because they are the producers of organic matter in fresh water, utilizing light energy and dissolved salts in building up new organic materials. As a general rule the abundance of sub-aqueous life is correlated both with the abundance of algæ and also with the amounts of certain mineral nutrients which are likely to limit their growth. The concentrations of bicarbonates, of nitrates and of phosphates are particularly important in this respect; but in some cases, as in some of the English Lakes, the continued growth of the diatom, *Asterionella*, is apparently limited by depletion of silica, which must exceed a concentration of 0·5 parts per million. There is also some evidence that the presence of high proportions of blue-green algæ in a water can be correlated with an abundance of dissolved organic matter.

Although there are many gaps in our knowledge of the factors which make for algal abundance, it is quite clear that as a general rule certain algal types are indicative of certain water conditions. It is known, for example, that the course of recovery from organic pollution in a stream can be traced by the sequence of algæ found below the pollution source. The influence of the dissolved salts on the algal flora is equally evident in unpolluted waters. In mountain regions, as in some Connemara lakes studied, the different floras characterize the more calcareous waters, and there are distinct elements indicative of peaty waters; while it was long ago noticed by Dr. G. S. West that the faintest traces of pollution by animal fæcal matter results in an abundance of diatoms. In fact, the organic life of a body of water is far more sensitive to traces of pollution than is usually supposed. The biological character of a piece of water depends so much on salts like nitrates and phosphates, the oxidized products of organic matter, that even traces of a completely oxidized sewage effluent usually suffice to change the flora and fauna qualitatively, and they will certainly enrich it quantitatively.

It follows from these facts that the biological analysis of the algal flora is capable of giving information of great value as to the quality of a water supply. At the same time, the recognition of the importance of the reservoir as a biological system would do much to simplify the water engineer's problems, and it may be useful to outline the problem from this point of view. Any deep body of water consists of two depth zones, an illuminated zone producing algæ and organic matter and well aerated as a result of photosynthesis, and a deep zone in which organic matter is broken down and oxygen is consumed. The rate of the latter processes is normally highest at the surface of the bottom mud, and consequently, as the temperature rises, the mud and the water above it may become devoid of oxygen or *anaerobic* whenever there is a large supply of organic matter. Under anaerobic conditions, nutrient salts rapidly diffuse from the mud to the water, ultimately to become available once more for plant growth in the surface layers of the water. If, however, conditions remain such as to maintain a higher oxygen supply at the mud surface, little or no diffusion of nutrient salts to the supernatant water is possible. The development of anaerobic conditions at the mud surface thus greatly increases the rate of circulation of plant nutrients, and especially the size of the vernal algal phase. The matter has a considerable bearing both on reservoir design and filtration difficulties.

It seems clear that the reservoir form ought to be one of low surface volume ratio designed to avoid oxygen deficiency in the lower layers, with an oxygen reserve sufficiently large to give a margin over the summer oxygen consumption, while the small surface should allow comparatively little production in the surface layers. Pertinent data here would presumably be obtained from estimates of the 'biological oxygen demand' and the potential algal or zooplankton production.

The development of oxygen deficiency in the deeper waters of a reservoir has direct effects on the water quality, as well as the indirect ones which result finally in greater algal production. One of these is that ferrous iron compounds appear in solution. These are at some later stage oxidized and redeposited in the ferric state, often in the pipes of the supply system. The processes involved are catalysed by certain iron bacteria, and they not only lead to the blocking of supply pipes but also to the unsightly staining of bathroom furniture.

Equally common under these conditions of oxygen deficiency is the presence of hydrogen sulphides or of other metallic sulphides, with particularly unpleasant smells. These cause great trouble in some calcareous waters containing much organic matter, and they have been a particular source of trouble in the filter beds of tropical and sub-tropical regions.

It is evident, from whatever angle it is approached, an important biological problem in water-works is that of reducing production. In southern and eastern England, where the drainage water is mainly from fertile land, the water works engineer must, if surface water is to be used, resign himself to the need for filtering off large quantities of algal and other organic material. In this case, topography and the need for bacteriological and chemical control of the product usually prevents even an approach to the ideal in reservoir form, while the use of the drainage area for agriculture prevents any attempt to sterilize it or reduce the productivity of the inflowing waters. It can be asked of the freshwater biologist that he forecasts the probable periods of greatest load in the filtering plant, a possibility dependent upon the recognition and maintenance of a seasonal rhythm in algal growth as well as an increased knowledge of the physiology of the organism concerned.

It is, however, also reasonable to inquire whether these steps wholly exhaust the possibilities. A profitable line of inquiry would be to consider whether the intensity of production at peak periods could be reduced and spread out over a longer period or diverted into other channels.

A reduction in algal growths has usually been brought about by the use of algicides, of which copper sulphate is most popular. There is some justification for employing such methods to retard algal growth, but little or none, other than dire necessity, for using them to destroy heavy growths, for the result is almost certainly to result in overtaxing the oxidizing agencies in the reservoir or filtration system, leading to the establishment of anaerobic conditions. In practice, moreover, copper sulphate is known to have other disadvantages; one of them is that more resistant algæ replace the earlier growths, and in some cases these are small enough to pass through filters. A second disadvantage is that there is an increase in the sulphur content of the bottom mud, and when oxygen deficiency develops, the bottom water acquires a high concentration of sulphides. To this agency, also, has been ascribed the later appearance, in some quantity, of sulphur bacteria.

Particularly striking effects are due to these organisms when they are pigmented forms such as *Rhodococcus*, which at times may colour water pink.

From the point of view of water supply, north-western Britain has the great advantage of being an area of high rainfall, of mountain and moorland, and of soils and water of low fertility. The control of reservoirs in such an area presents quite a different series of problems. The first of these is that though the initial fertility of a water is almost always low, yet it is already known that after 30–50 years reservoirs have developed algal production to a high degree. This falls in line with the discovery that certain of the English lakes are accumulating nutrients (nitrogenous materials, for example). In summer more nitrogen enters the lake by the inflows than goes out down the outflow, and it seems that this state of affairs must be not infrequent. Moreover, in winter, the amount of available nitrogen (for example, nitrates) in a natural water is generally at a maximum. If we store this water instead of allowing it to escape to the sea we are, in effect, putting a trap for plant nutrients into the system, so that the annual production is in any case likely to rise.

It seems clear, therefore, that any measure which will tend to reduce fertility in these waters will be valuable. Even if it were only possible to remove a small percentage of the circulating nitrogen and phosphorus, for example, it might suffice to remove the annual accumulations in the lake system.

The question of how to remove part of the annual crops of organic matter becomes a very important one in this particular instance. The obvious way of cropping a reservoir and of obtaining some financial return for the labour involved is to take a crop of fish or of some other cash product from it. The annual crop should equal the annual gains of nitrogen, for example, or else should help dissipate it. From the point of view of the economy of the country as a whole, indeed, the whole of the valuable nitrogenous compounds could profitably be removed from the water. What are the conditions and limitations of this ideal? In effect, the production of organic matter in water passes along a series of food chains—starting generally from algæ, passing by various stages, such as plankton, molluscs and insect larvæ, for example, into fish. Now in each of these steps there is a considerable loss of production. To take a more familiar example, a mature sheep has eaten about ten times its own weight during its growth and development. Thus if this sort of difference is usual, a food chain, containing four steps: *a* (algæ), *b* (insects), *c* (small fish), *d* (larger fish), would give relative productions as percentages of the initial production mechanism of:

(*a*) 100, (*b*) 10, (*c*) 1, and (*d*) 0·1.

(It is, however, perhaps likely that the ratio of weight of food to weight produced is less than that used; about 5 to 1 has been suggested for freshwater creatures.) Generally speaking, water-works practice does not favour fish production in their impounding reservoirs, and to this extent it limits the possible food chains. Clearly, also, the method of operation collects the primary producers (algæ), and so has to deal with the largest weights, though at the same time it probably removes the largest amounts of carbon and nitrogen. However, the algal maxima are short-lived, and it would be advantageous to be able to crop at any time. This means using long-lived creatures for crop-taking.

In contrast, those interested in fish production may obtain higher yields by the shortening of the food chains. It would, for example, greatly increase the yield if, say, the fish (*c*) could be taken rather than another piscivorous fish (*d*); and better still, herbivorous species of fish should give higher production than any carnivorous species.

The piscicultural and the water-works problems are thus both different aspects of one which has equally important bearings on our natural economy to-day—for in these lean times, we are deeply concerned with obtaining the maximum yield from our diminishing acres. It may, therefore, be interesting to collect data comparing the productivity of water and of land in comparable terms.

	Yields in lb. per acre
Land:	Meat only, 190.
	Wheat, 1,800–2,000*.
	Beet (as sugar), 3,000*.
	* Approximately equivalent to *dry* weight.
Water:	Thames water—*c.* 1,400–2,000* maximum algal.
	Lake Mendota—Total plankton, *c.* 10,000*.
	Algæ in water, say, 6,000*.
	Submerged shore-weeds, 1,500–1,800*.
	* Dry weight.
Fish:	6– 10, Alpine lakes.
	170–180, Illinois river.
	180–200, carp ponds (manured).

The estimates for Lake Mendota plankton assume that it is renewed weekly. I think this may be two or three times too often. The data for average dry weight of green plants on the shores of this lake suggest that algal production in the plankton might be 2–3,000 lb. per acre as dry weight, a somewhat similar figure to the estimate for vernal production in Thames water.

It will be seen that the productivity of fertile waters approaches that of the fertile lands from which they drain and the richness of which they contain. From the point of view of conserving natural resources there is much to be said for exploiting the reserves of nitrogen and phosphorus which are otherwise being washed away to the sea. It may be that when we use fertile surface waters for water supply purposes, some system of preliminary crop-taking might be introduced—shallow reservoirs the bottom mud of which could be often removed, or used for a system of water-meadows or for fish-cropping. At any rate, it seems that the desirable biological control of water resources involves consideration of these matters.

TOXIC PROPERTIES OF ω-FLUORO-CARBOXYLIC ACIDS AND DERIVATIVES

By DR. B. C. SAUNDERS
University Chemical Laboratory, Cambridge

WE have already reported[1] upon the highly toxic nature of fluoroacetic acid, FCH_2COOH, and its derivatives. The present communication gives an account of further work on the toxicity of allied compounds. The earlier part of the present investigation was carried out under the ægis of the Ministry of Supply during the War, and reports were submitted to that Ministry from time to time and were made available to American workers. The more recent parts of the work have been sponsored by the Imperial Chemical Industries, Ltd. (General Chemicals, Widnes). We are grateful, therefore, to the Chief Scientist, Ministry of Supply, for permission to publish the details of the reports to the Ministry of Supply, and to Imperial Chemical Industries, Ltd., for grants which have enabled us to continue the work.

Methyl fluoroacetate[1,2] was shown to be a convulsant poison and highly toxic by inhalation and by injection; the L.D. 50 for subcutaneous injection into mice being of the order of 7 mgm./kgm., and the figure for intravenous injection into rabbits being 0·25 mgm./kgm. The toxicity figures for fluoroacetic acid were of the same order, and the symptoms produced by the free acid were identical with those produced by the methyl ester.

We then demonstrated that a large variety of derivatives of fluoroacetic acid exhibited the same order of toxicity as that shown by the acid itself. For example, $FCH_2COOC_2H_5$, $FCH_2CONHCH_3$, and $(FCH_2CO)_2O$ were almost equally toxic. Fluoroethyl alcohol, FCH_2CH_2OH, and the aldehyde, FCH_2CHO, were also of the same order of toxicity, whereas fluorochloroethane, FCH_2CH_2Cl, was non-toxic. These results indicated that a compound which could give rise to fluoroacetic acid either by hydrolysis or oxidation was toxic[3]. In other words, the toxic principle appeared to be fluoroacetic acid, or the fluoroacetate ion.

American workers[4] reported that esters of 2-fluoropropionic acid, FCH_2CH_2COOH, were non-toxic, and that esters of 3-fluorobutyric acid were toxic. In June 1944 we announced[5,6] that we had synthesized ethyl 5-fluorohexoate, $F(CH_2)_5COOC_2H_5$, a stable colourless liquid. We found that the toxicity of this compound was very high, and by injection into mice had an L.D. 50 of about 4 mgm./kgm. Ethyl 5-fluorohexoate was therefore about three times as toxic as methyl fluoroacetate (per molecule).

We showed in April 1943 that 2-fluoroethyl fluoroacetate was about twice as toxic as methyl fluoroacetate by inhalation[7]. It seemed likely then that the 2-fluoroethyl ester of 5-fluorohexoic acid might be a compound of outstanding toxicity, and this proved to be the case[8]. This compound was made by the method as outlined below:

$$Br(CH_2)_5COOH \xrightarrow[H_2SO_4]{FCH_2CH_2OH} Br(CH_2)_5COOCH_2CH_2F$$

$$\xrightarrow{AgF} F(CH_2)_5COOCH_2CH_2F.$$

The L.D. 50 of 2-fluoroethyl 5-fluorohexoate as determined by subcutaneous injection into mice was 2·5 mgm./kgm., that is to say that it is about eight times as toxic as methyl fluoroacetate (per molecule).

For purposes of comparison, the toxicity of methyl fluoroacetate, 2-fluoroethyl fluoroacetate, ethyl 5-fluorohexoate and 2-fluoroethyl 5-fluorohexoate are shown in the accompanying table. The inhalation figures are for a 10 minutes exposure. The toxicity of 2-fluoroethyl 5-fluorohexoate, though high by inhalation, was not quite so pronounced as might have been expected; but this is probably accounted for by the fairly low volatility of the compound. For purposes of comparing the toxicities of compounds of low volatility, it is probable that injection experiments are more reliable than inhalation experiments.

Compound	Mice		Rabbits		Rats	
	L.D. 50 sub.-cut. inject. (mgm./kgm.)	L.C. 50 Inhal. (mgm./l.)	L.D. 50 intra-venous inject. (mgm./kgm.)	L.C. 50 inhal. (mgm./l.)	L.D. 50 intra-mus. inject. (mgm./kgm.)	L.C. 50 inhal. (mgm./l.)
Methyl fluoroacetate	7–10	3·2	0·25	0·025–0·05	2·5	0·3
Ethyl 5-fluorohexoate	4	0·2	0·2–0·5		2·3	
2-fluoroethyl fluoroacetate	8·5	0·45		0·05		0·15
2-fluoroethyl 5-fluorohexoate	2·5	0·15	0·1–0·2	0·02–0·05	1·8	0·2

The very high toxicity of 5-fluorohexoic acid and its derivatives is interesting, since by a process of beta-oxidation it could readily give rise to fluoroacetic acid in the body. Similar remarks apply to 3-fluorobutyric acid prepared by American workers. On the other hand, 2-fluoropropionic acid could not, presumably, be oxidized by the beta-oxidation process to fluoroacetic acid.

In order to ascertain more completely whether this striking alternation in toxic properties was fortuitous, we then prepared other ω-fluoro-carboxylic esters, none of which had previously been described[8]. Ethyl-4-fluorovalerate, $F(CH_2)_4COOC_2H_5$, was shown to be non-toxic. On the other hand, we showed that ethyl 9-fluorodecoate, $F(CH_2)_9COOC_2H_5$, was extremely toxic in accordance with expectation, but the toxicity figures were considerably greater than would have been anticipated on the β-oxidation theory. In fact, molecule for molecule, it was much more toxic than methyl fluoroacetate. It may be argued that because of its longer chain, the fluorodecoate would have a higher 'fat : water' distribution, and would therefore pass more rapidly than methyl fluoroacetate through the cell membrane, and there break down giving a higher intracellular

Compound	L.D. 50 for injection into rabbits
FCH_2COOCH_3	0·25 mgm./kgm. (in saline)
$F(CH_2)_9COOC_2H_5$	0·2 mgm./kgm. (in propylene glycol*)

* The fluorodecoate would probably be even more toxic in saline, as methyl fluoroacetate appears to be rather more toxic in saline than in propylene glycol.

concentration. It cannot, therefore, be stated with certainty that β-oxidation is the only factor or even the major factor concerned with the alternation of toxic properties.

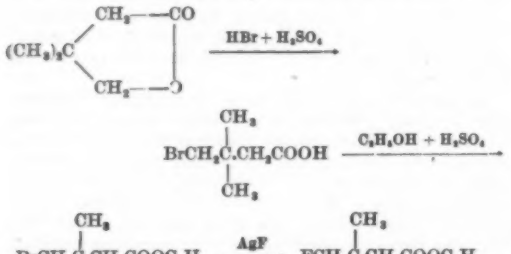
It is also important to keep in mind the fact that 2-fluoroethyl fluoroacetate, $FCH_2COOCH_2CH_2F$, was found to be twice as toxic (by inhalation) as methyl fluoroacetate weight for weight[7]. The rate of hydrolysis of the two substances was found to be similar. One mol. of the former gives rise to one mol. of fluoroacetic acid and one mol. of fluoroethyl alcohol (oxidizable to fluoroacetic acid). Therefore if hydrolysis and oxidation were the major factors concerned, then 2-fluoroethyl fluoroacetate should possess approximately the same toxicity as methyl fluoroacetate (weight for weight). This may indicate that the 2-fluoroethyl fluoroacetate molecule can exert a toxic action *per se*, independent of any subsequent degradation.

In line with this observation, we found that 2-fluoroethyl 5-fluorohexoate was more toxic than the corresponding ethyl ester (by injection). On the other hand, 2-fluoroethyl 9-fluorodecoate does not appear to be more toxic than the corresponding ethyl ester. This result requires further investigation.

We have recently added to the series by the synthesis of ethyl 10-fluoroundecoate, $F(CH_2)_{10}COOC_2H_5$, which was found to be non-toxic, and of ethyl 7-fluorooctoate and 11-fluoroduodecoate, both of which proved to be highly toxic.

Acids Substituted in the β, and in the α and β, Positions

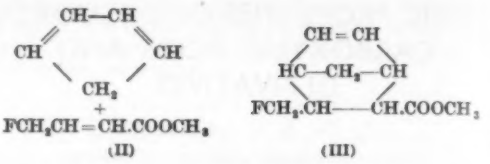
The problem was then approached at a different angle. As already stated, 3-fluorobutyric acid is known to be highly toxic, a fact which could be accounted for on the β-oxidation theory. The process of β-oxidation could presumably be stopped by effectively 'blocking' the β-position in the chain. We therefore synthesized ethyl 2 : 2-dimethyl 3-fluorobutyrate (I) according to the following scheme :



(I)

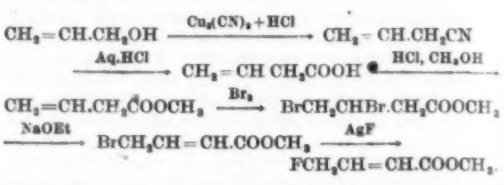
The compound (I) was found to be non-toxic as expected.

An independent method of approach consisted in 'fixing' carbon atoms 2 and 3 in the highly toxic 3-fluorobutyrate by making them form part of a ring system. Presumably the process of β-oxidation would be inhibited in the new compounds, which should therefore be non-toxic. For this purpose we carried out a Diels–Alder condensation of cyclopentadiene and methyl 3-fluorocrotonate (II), and obtained the compound (III), which was, in accordance with expectation, non-toxic.



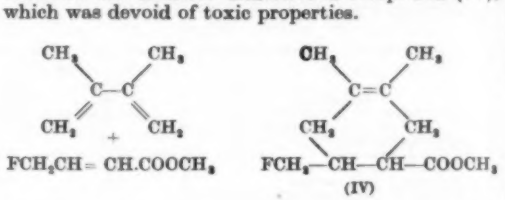
(II) (III)

It should be mentioned here that the crotonate (II) had been shown by American workers to be highly toxic. For the present investigation we prepared the compound as follows :



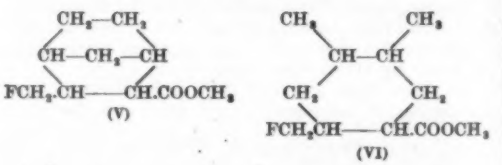
The methyl bromocrotonate was also prepared by the action of N-bromosuccinimide on methyl crotonate.

We also effected the condensation between 2 : 3-dimethylbutadiene and methyl 3-fluorocrotonate and obtained the hitherto undescribed compound (IV), which was devoid of toxic properties.



(IV)

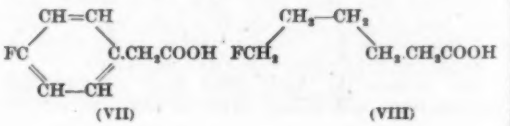
It was found that compounds (III) and (IV) could be hydrogenated under conditions which did not remove the fluorine atoms, and the fully saturated compounds (V) and (VI) were also found to be non-toxic.



(V) (VI)

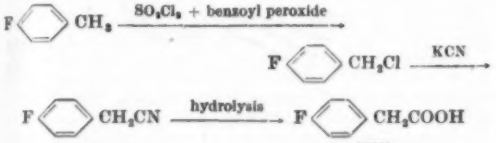
Thus five compounds in all were synthesized, containing the skeleton of the toxic 3-fluorobutyric ester. They possessed structures of such a kind that β-oxidation would be unlikely in the animal body. The fact that these new compounds were non-toxic is some evidence in support of the β-oxidation theory. On the other hand, if their toxic properties had been comparable with that of the parent acid, it would have been necessary to have abandoned the β-oxidation theory.

One further compound may be mentioned in this connexion, namely, *p*-fluorophenylacetic acid (VII), which has the carbon skeleton of the highly toxic 5-fluorohexoate (VIII) :



(VII) (VIII)

The compound (VII) was found to be non-toxic, and cannot, of course, be oxidized to fluoroacetic acid. *p*-Fluorophenylacetic acid had previously been prepared in small quantity by Dippy and Williams[9] by a rather laborious process. We developed a new synthesis of the compound (VII) in good yield as follows :



(VII)

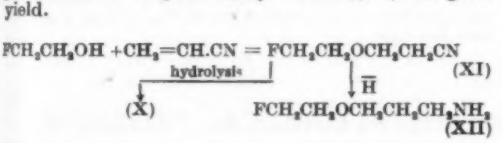
ω-Fluorocarboxylic Acids Containing a Hetero-Oxygen Atom

We have also devised another method[6] which may throw light on the phenomenon of alternating toxicities and the possible connexion with the β-oxidation process. Here the principle was to replace a CH_2-group at some appropriate point in the chain by an oxygen atom, and then to compare the toxic action of the new compound with that of the parent ω-fluorocarboxylic acid. Thus whereas 5-fluorohexoic acid (IX) and its derivatives are extremely toxic, the corresponding oxygen compound (X) had an L.D. 50 for injection into mice of only 70 mgm./kgm.

$FCH_2CH_2CH_2CH_2CH_2COOH$ (IX) L.D. 50 : 4 mgm./kgm. for ethyl ester.

$FCH_2CH_2OCH_2CH_2COOH$ (X) L.D. 50 : approx. 70 mgm./kgm.

Several compounds of this type have been prepared by a novel synthesis depending upon the cyano-ethylation of the appropriate fluoro-alcohol. Thus the cyano-ethylation of fluoroethyl alcohol (prepared according to the method of McCombie and Saunders[10]) gave 2-fluoro-2′-cyanodiethyl ether (XI) in good yield.

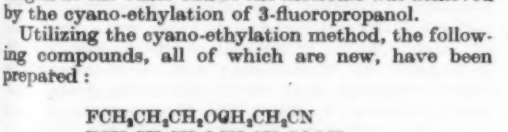


It was found possible to reduce the ether (XI) to the corresponding primary amine (XII) by means of Raney nickel and hydrogen, without removing the fluorine atom. The conditions for the reduction were critical and were arrived at only after several failures. This then allowed of the possibility of lengthening the chain at one end of the molecule. Increase in length at the other end of the molecule was achieved by the cyano-ethylation of 3-fluoropropanol.

Utilizing the cyano-ethylation method, the following compounds, all of which are new, have been prepared :

$FCH_2CH_2CH_2OCH_2CH_2CN$
$FCH_2CH_2CH_2OCH_2CH_2COOH$
$FCH_2CH_2CH_2OCH_2CH_2COCl$
$FCH_2CH_2CH_2OCH_2CH_2CH_2COOC_2H_5$
$FCH_2CH_2OCH_2CH_2COCl$
$FCH_2CH_2OCH_2CH_2CH_2COOC_2H_5$

The acid chlorides were converted into the esters of the higher acids by the Arndt–Eistert reaction :



The physiological examination of these ethers is being undertaken at present.

Summary

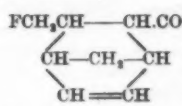
(1) A striking alternation in the toxic properties of ω-fluorocarboxylic esters has been demonstrated as follows :

FCH_2COOR	toxic
FCH_2CH_2COOR	non-toxic (American workers)
$F(CH_2)_3COOR$	toxic (American workers)
$F(CH_2)_4COOR$	non-toxic
$F(CH_2)_5COOR$	toxic
$F(CH_2)_7COOR$	toxic
$F(CH_2)_9COOR$	toxic
$F(CH_2)_{10}COOR$	non-toxic.
$F(CH_2)_{11}COOR$	toxic

These results are discussed from the point of view of β-oxidation in the animal body. The conclusion is that while β-oxidation may be a factor in accounting for this alternation of properties, other important factors are also involved.

(2) Ethyl 2 : 2-dimethyl 3-fluorobutyrate, $FCH_2C(CH_3)_2CH_2COOC_2H_5$, in which the β-position is 'blocked', is found to be non-toxic.

(3) Methyl 2-fluoromethyl-3 : 6-endomethylene-Δ^4-tetrahydrobenzoate,



and three other related compounds in which the α and β positions are 'fixed', are non-toxic.

(4) We have been able to introduce a hetero-oxygen atom at appropriate points in the chain of ω-fluorocarboxylic acids by methods depending ultimately upon the cyano-ethylation of the appropriate fluoro-alcohol. Thus compounds of the general type $F(CH_2)_mO(CH_2)_nCOOH$ have been obtained. The toxic properties of these compounds are at present being examined.

These investigations were carried out by F. J. Buckle, F. L. M. Pattison and B. C. Saunders. We express our thanks to Imperial Chemical Industries, Ltd., for research studentships to two of us (F. J. B. and F. L. M. P.). We are indebted to Mr. K. J. Carpenter and to Dr. W. J. O'Connor, who have performed the animal experiments.

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DUNDEE MEETING OF THE BRITISH ASSOCIATION, AUGUST 27–SEPTEMBER 3

As has already been announced, the British Association will meet at Dundee during August 27–September 3, and a preliminary programme referring to general features of the meeting has been issued. The following notes, from the recorders of the various sections, amplify the information given there.

Section A (*Mathematics and Physics*). In his presidential address, Sir Edward Appleton will deal with the way in which radio has been used in communication and also as a method for investigating natural phenomena, by study of the reflexions from meteors and the reception of radio 'noise' from the sun and Milky Way. The session on September 2, devoted to "Coal as a Source of Heat and Power", will hear Sir Charles Ellis, who will be followed by contributors from the Fuel and the Building Research Stations on the efficient use of fuel and domestic heating systems. Prof. J. D. Bernal will review the question of coal economy, and Prof. D. M. Newitt will speak about the use of oxygen in carbonization processes and the storage of gases in liquid form. The British Coal Utilisation Research Association will deal with the combustion of coal in fuel beds. The discussion of modern methods of computation will include a general survey and a description of some large American machines.

Section E (*Geography*) will devote a whole day to a discussion of Scottish problems from the geographer's point of view. The National Atlas and urban geography will each have a morning. There will be an exhibition of maps produced by the Scottish Department of Health and the Ministry of Town and Country Planning.

Section F (*Economics*). Current economic difficulties will receive particular attention. The presidential address is to be on the "Conditions of the Economic Outlook", and there will be papers on "The Significance of the New Issue Market for the Finance of Industry", "Land Compensation", "Social Accounting", "Profit and Enterprise", "Proposed Code of Industrial Management". A joint meeting with Section J (Psychology) will consider "Incentives in Industry".

Section G (*Engineering*). An outstanding feature will be a series of short papers by junior engineers: thirty minutes is allotted to each speaker for his paper and the ensuing discussion. In preparation for the afternoon visits, the last item of the morning programme will be a summary of what is to be seen.

Section H (*Anthropology*) will hold a symposium on problems of "Culture Change", to which members of the staff of the London School of Economics will contribute. The archæological side will discuss Pleistocene chronology under the title "Dating the Past". Papers are to be presented on a variety of subjects, including the technique of excavation, the education of the totally deaf child, the organisation of folk-life studies, reconstruction in the Naga Hills, and recent discoveries of fossil Hominoidea in South Africa.

Section I (*Physiology*) will hold a joint meeting with Sections H and J to discuss "Man and the Machine", with the object of showing how the physiology, anatomy and psychology of the man should be considered in the design of the machine he is to use. Two other meetings include Section J, when "Aviation Physiology" and "Climate and Health" will be discussed. On August 29 Sir Alexander Fleming will open a symposium with Sections B and K on "Penicillin and other Antibiotics". The use of tracer elements will be the subject of a meeting with Section B on the morning of September 2. During the meeting a Children's Lecture on "Colour" will be given by Prof. H. H. Hartridge.

Section J (*Psychology*). The contributions are mainly of practical interest, industrial and educational applications being especially prominent. The Section joins with others in discussing "Man and the Machine", "Allocation to Secondary Education" and "Incentives in Industry". The sectional meetings include symposia on "Selection for Management", "Public Opinion Surveys", "Rehabilitation of an Industrially Depressed Area", "Changes in Abilities with Age" and "The Scientific Study of National Character". Dr. S. J. F. Philpott's presidential address is "Man's Adaptability".

Section L (*Education*). Miss Grier's presidential address will be on the evolution of secondary education. Miss Lambert will present a paper on the "Problems of Selection Technique at the age of Transfer to Secondary Schools". There will be a discussion on adult education in the Services.

Section M (*Agriculture*). The first session will be a joint one with Sections B and D to discuss insecticides. Papers will be presented (by Drs. H. G. Thornton, M. C. Rayner and A. P. Evans) on three aspects of soil biology—the roles of bacteria, mycorrhizas and earthworms in the economy of the soils and the maintenance of fertility. A session is devoted to recent advances in the control of animal diseases, and at the final session the Right Hon. Walter Elliott, M.P., Sir Jack Drummond and Mr. H. D. Walston will discuss, from the points of view of the agriculturist, nutritionist and economist, respectively, the vitally topical problem: How far could and should Britain feed herself? In his presidential address, Dr. W. G. Ogg will speak on "Soil and Health", and will describe recent studies on the effect of soil conditions on the health of plants and animals.

METALLURGICAL PROBLEMS INVOLVED IN THE GENERATION OF USEFUL POWER FROM ATOMIC ENERGY*

The design of even the simplest atomic energy reactor, the water-cooled carbon pile using natural uranium, presents many awkward technical problems. Metallic uranium has properties which make it a difficult material to work with. It melts at about 1,150° C.; but below this temperature it undergoes two transitions, with unusually large volume changes. It is very reactive chemically, and readily attacked by water. For these reasons, and to retain the radioactive fission products, the uranium rods in a pile have to be enclosed in gas-tight sheaths, of materials which are good heat conductors, non-corrosive and do not absorb neutrons appreciably.

* Substance of the May Lecture before the Institute of Metals delivered by Sir Wallace Akers, C.B.E., on May 21.

These conditions limit the choice to beryllium and aluminium. Beryllium would be excellent, but so far nobody has succeeded in making tubes from it. Aluminium has therefore to be used, although it is not ideal, as water tends to form surface films, which interfere with the heat transfer. The uranium and graphite have to be purified to a degree hitherto unknown on such a scale; the most important impurity is boron, which seems to be present in very small quantities in almost all reagents. The preparation of aluminium-sheathed rods of uranium of the required purity represents a metallurgical achievement of a very high order.

But even when these difficulties have been overcome, it is unlikely that water-cooled plants will produce useful power. In order to achieve a reasonable thermal efficiency, the water would have to be worked at a considerable pressure; the aluminium tubes would therefore have to be much thicker and would consequently capture too many neutrons. More promising is the use of liquid bismuth, or helium, both of which have very low neutron-capture cross-sections. Even then the pile would have to be very large and its design extremely critical; because the very narrow balance between the number of neutrons produced at fission and those left after capture by U238 and the various materials entering into the construction of the pile necessitates the cutting down of the escape of neutrons and their loss in impurities to a minimum.

Much smaller reactors and greater latitude in design become possible, if, instead of ordinary uranium, material enriched in fissile content is employed. The use of uranium enriched in U235 is not economical because of the high cost of separation, but it is feasible to utilize the production of plutonium by capture of neutrons in U238. This may be of vital importance for the supply of fissile fuel, because if it could be arranged that, for every nucleus of U235 burnt up, one plutonium nucleus were produced, the total number of fissile nuclei would remain constant; in fact, their proportion would increase steadily as U238 is being used up. One cannot say at present whether it would be possible to go further than this and produce more plutonium nuclei than of U235 burnt up. If such 'breeding' of plutonium could be achieved, the problem of availability of supplies of fissile fuel would be solved immediately.

In this respect the production of U233 from thorium is more promising. This is done by placing thorium in the outer layers of a graphite-uranium pile so that it is exposed to neutrons which would otherwise escape. The possibility of 'breeding' is in this case more pronounced, since the number of neutrons ejected at fission of U233 may be sufficiently high to make it possible to build a reactor in which more nuclei of U233 are formed than are burnt up. If this turns out to be practicable, then, having once made some U233 from thorium placed in a uranium pile, we could dispense with natural uranium altogether and continue to produce U233, and generate power, using only thorium as a raw material. Furthermore, this would enable us to utilize, by conversion to plutonium, any U238, from graphite-uranium piles, which became useless owing to the impoverishment in U235.

When will atomic energy be available? As a pure guess it would seem that an experimental plant will be running in the United States by 1949, and that in five to ten years there will be some fairly large power stations generating electricity in various parts of the world. It is impossible to say anything definite about the economics of these plants. The figures quoted recently in the United States depend on several assumptions and data not available in Britain; but for more remote places, without fuel resources, atomic power may well be economical even now. For example, an atomic energy power station might be built to provide power and heat for a large airport near the North Pole, to shorten many important air routes.

The consumption of nuclear fuel is extremely low; one kilogram of fissile material liberates as much heat as the burning of 2½ million kilograms of high-grade bituminous coal. The amount of electrical energy generated in Great Britain is about 50,000 million kWh. per annum. If the heat generated in fission could be utilized with a thermal efficiency of 27 per cent, the consumption of fissile material needed to produce this amount of electrical energy would be about 7½ tons per annum. If only U235 were burnt, the quantity of ordinary uranium required would be about 1,000 tons per annum, which is just what the total world output of uranium was in 1939. Although the production has since then certainly increased, it is clear that uranium has no future for power production if only U235 could be utilized. But if a substantial part of U238 or, still better, if thorium could also be used, then the figures become reasonable.

Contrary to common belief, uranium and thorium are far from being among the rarest elements. In the rocks composing the globe there are on the average about 4 parts per million of uranium and 11½ of thorium, as compared with 0·5 of mercury and only 0·005 of gold. But unfortunately uranium does not occur frequently in large enough concentrations; thorium is rather better in this respect. Granites and rhyolites contain 10 to 20 grams of uranium plus thorium per ton; their 'calorific' equivalent is thus 25 tons of coal per ton of rock; but the very complex nature of the compounds in which uranium and thorium exist in them makes it impracticable to mine and extract the fuel from rocks.

AN INTERNATIONAL UNION OF FAMILY ORGANISATIONS

A MARKED tendency in educational and social thought of recent years, and a tendency accentuated by the strains to which society has been subjected by the War and the ensuing peace, has been the renewed emphasis placed on the family as the basic social unit and as the most powerful educational influence acting upon the individual. It is therefore not surprising that in various countries efforts have been made to set up organisations to co-ordinate activities relating to family life; organisations such as the National Council on Family Relations in the United States, the Family Relations Group in Great Britain, and the Union Nationale des Associations Familiales in France. The next needed step was clearly the formation of some machinery for international information and documentation, and the building of this machinery has now been started.

In Paris, during June 22–29, there was held an International Congress on the Family and on Population. It was attended by some two hundred delegates from twenty-four countries and, although few of the delegates attended with the official support of their

Governments, there seems little doubt that the Congress was fairly representative of the main streams of thought in most of the important countries of the world.

This very fact, indeed, was responsible for what at first appeared to the writer to be a weakness in the Congress. When some delegates were enthusiastic about large families and others little concerned with mere family size, when some were interested in the problems and techniques of family planning and others condemned it as immoral, when some represented still quite patriarchal countries and others countries in which women were fully recognized as the equals of men, it was difficult to get down to any detailed discussion or expert examination. In truth, it could not be claimed that this Congress achieved anything very important in the way of settling the problems of family life. It did, however, provide an opportunity for the exchange of information and widely differing views on housing and homemaking; sex education, marriage guidance and general education for family life; the role of women in general (and mothers in particular) in society; family allowances and other social measures for the strengthening of family life; the role of family organisations in national life, and so on.

Out of this exchange there emerged, despite all differences of opinion, a widespread and deep desire for international co-operation. Most delegates felt that they could learn much, and perhaps most of all from those from whom they differed most widely. Towards the end of the Congress, this diffuse desire for international co-operation gradually crystallized into a determination to set up an international organisation and, at the final session, a resolution to this effect was passed unanimously.

The new organisation is to be called the International Union of Family Organisations; but it was clearly recognized that all decisions as to structure and programme could at present be purely provisional. The British delegates, in common with those from most other countries, felt that they had no mandate whatsoever to commit their countries or even the organisations they represented to anything very concrete. Equally, however, they felt that it would be a great pity to allow this very representative gathering to disperse without forming at least an embryonic organisation. A provisional international committee was therefore set up, a Swiss delegate was appointed as provisional president, and a French delegate as provisional secretary. It was agreed that vice-presidents should, if possible, eventually be appointed from the United States, Great Britain, France, 'Eastern Europe' (by which the U.S.S.R. was generally understood to be meant), Scandinavia, South America, the Near East and the Far East; and, no doubt, it was by an oversight (for these provisional arrangements were necessarily made hurriedly) that Africa and Australasia were not included in this list. Finally, it was agreed that the International Union should be open to all countries, including those not represented at the Congress, and that every effort should be made to work closely with U.N.O. and U.N.E.S.C.O. It is encouraging to be able to report that an observer from U.N.O. welcomed the establishment of the International Union.

Whether the future will see a great strengthening of the new International Union of Family Organisations, or whether it will see its gradual withering, it is as yet impossible to say. Everything depends upon whether the action of the delegates is ratified when they report back to their respective national organisations. One most encouraging fact, however, is that throughout the world to-day there is great interest in the problems of family life. Catholics and Protestants, Capitalists and Communists, all, in their different ways, recognize the importance of the family, and in this lies great hope.

CYRIL BIBBY

NEWS and VIEWS

East African Agricultural and Forestry Research: Dr. B. A. Keen, F.R.S.

DR. B. A. KEEN has been appointed director of the new East African Agricultural and Forestry Research Organisation. The Organisation will work in close association with the corresponding Veterinary Organisation and the Agricultural Departments of Kenya, Uganda, Tanganyika and Zanzibar. For many years Dr. Keen was assistant director and head of the Physics Department at Rothamsted Experimental Station. During 1929–31, at the request of the Government of India, he was seconded as director of the Imperial Agricultural Research Institute to reorganise it. During 1943–45, he was scientific adviser to the Middle East Supply Centre. In 1946 he revisited Palestine to advise on the organisation needed for rural development and also went to West Africa as chairman of the United Kingdom Government Mission to inquire into the production of vegetable oils and oil seeds. Since February 1947 he has been touring East Africa at the invitation of the Governors' Conference to examine agricultural problems and research needs.

Recordings at Kew of the Brest Explosion

MR. J. M. STAGG, of the Kew Observatory, Richmond, Surrey, writes that the effects of the explosion of a cargo of nitrate in Brest harbour on the evening of July 28 were clearly recorded on one of the seismographs and on four barographs at the Observatory, which is 480 km. from Brest. The seismograph, a short-period, vertical component instrument, recorded the first effect at 16h. 48m. 52s. G.M.T. with a second pulse nine seconds later. The biggest amplitude occurred at 16h. 49m. 05s. and the whole disturbance lasted about one minute. The character of the effect on the seismograph closely resembled the effects produced by bomb explosions, flying bombs, etc., in the neighbourhood of the Observatory during the War, when, for the most part, the disturbances were due to airborne sound waves. That the seismograph disturbance was due to the explosion air wave and not to true earth movements is supported by the times of the disturbance recorded by the Kew barographs, including a very sensitive microbarograph. All four instruments showed a sudden pulse (about one millibar) of very short duration in both directions, the mean of the times being 16h. 49m. 0s. ± 15s. The Kew records taken together put the time of the Brest explosion at about 16h. 25m. G.M.T.: there was no indication of an earth movement or an upper air sound wave.

Audibility of Members of Parliament

EXPERIMENTS are being conducted in the House of Lords, in which the House of Commons sits while the Lower Chamber is being rebuilt after destruction during the War, to improve the audibility of members. Comprehension of a speaker's words is low because the first major reflextion, on which reliance is placed by auditors, especially in the rear of a speaker, is scattered by the extensive wooden carving; moreover, the roof is too high to afford any useful reflexions. The acoustic problem is complicated by the premise that any speaker may jump up and address remarks, theoretically to the chair, but often elsewhere. Permission from the authorities has been obtained to install, as an experiment, three hollow tubes acting as hand-rails, one on each side of the House behind the Treasury and Opposition benches, the third in front of the Hansard and some Press reporters just over the Speaker's chair. Each tube is driven by a horn loudspeaker electro-dynamic driving-unit at one end, the other end having an acoustic termination to obviate reflexions. Along the pipe are small holes, so that reproduced sound from the existing system of microphones is emitted just below a member's ear, or in front of a reporter. It is unlikely that a considerable increase in general audibility can be obtained by any means; but the pipe scheme for low-level individual sound augmentation certainly helps the audition of poor speakers, and is of considerable help when the noise-level increases. In particular, the Press are much more certain of getting the remarks of the Speaker. Present trials will indicate whether the pipe system can be extended with advantage, and possibly incorporated in the new Lower Chamber.

Advisers to the Minister of Civil Aviation

LORD NATHAN, the Minister of Civil Aviation, has appointed the following to be his advisers in science, business and industrial relations: chief scientific adviser, Prof. George Temple; chief business adviser, Mr. Leslie Gamage; chief adviser on industrial relations, Lord Dukeston. Prof. Temple is professor of mathematics in King's College, London. He is also a member of the Aeronautical Research Council. He was seconded for specialist duties to the Royal Aircraft Establishment, Farnborough, during the Second World War. Mr. Leslie Gamage is vice-chairman and joint managing director of the General Electric Co., Ltd. For the past four years he has been president of the Institute of Export. He is a member of the National Civil Aviation Consultative Council, representing the Joint Air Transport Committee of the Association of British Chambers of Commerce, the Federation of British Industries and the London Chamber of Commerce. Lord Dukeston was the general secretary of the National Union of General and Municipal Workers. He represents the Trade Union Congress on the National Civil Aviation Consultative Council. He was president of this year's Trade Union Congress, and is the British Government member on the United Nations Organisation Commission to set up a Bill of Human Rights.

Royal Society Empire Scientific Conference

THE preliminary report of the Royal Society Empire Scientific Conference, June–July 1946, which has now been published by the Royal Society, includes the speeches at the opening ceremony with lists of the morning discussions, of the papers prepared for the Conference, of the delegates, etc. The summaries of the discussions given in this report detail the recommendations (see *Nature*, July 27, 1946, p. 136), many of which were afterwards endorsed by the Official Conference. The morning discussions surveyed first some outstanding problems in agricultural science in the Empire, including scientific needs concerned with the soil, the plant and the farm animal. Next some outstanding problems in medical science were discussed, including the physiological and psychological factors affecting human life under tropical conditions and in industry, and the etiology and control of infectious and transmissible diseases, particularly those which are insect-borne. The present state of the science of nutrition was discussed with particular reference to the special problems of the Empire, including the nutritional status of the indigenous peoples of the Colonies. Improvement of that status was recognized by the Conference as a part of general social and economic policy in the territories concerned, and the Conference strongly urged the need for integrating the efforts of producer, consumer, technical and administrative personnel in effecting improvements in nutrition.

Other discussions covered a variety of topics: modern methods of mapping and exploration by air, including the use of radio technique in ordnance survey with special reference to particular parts of the Empire; scientific information services and methods of improving the interchange of scientific workers throughout the Empire, including the future of the scientific liaison offices that were established during the War; Empire co-operation in the scientific field with existing and projected international organisations; physical standards of measurement, the collection of scientific records and material and risks involved in the distribution of plants, seeds and animals, and so on. A general statement on land utilization and soil conservation emphasizes the importance of erosion surveys, soil surveys, and investigations relating to the maintenance and improvement of soil fertility, and urges the importance of surveys to determine the present pattern of and trends in land use, as a basis for the maintenance of soil fertility, bearing in mind the conflict between agricultural and other interests. A discussion on the need for a co-ordinated survey of the mineral resources of the Empire led to a general statement urging the compilation of reliable data on mineral resources. Discussions on the natural products of the Empire and the chemical industries that are, or might be, based on them and on the post-war needs of fundamental research, the latter of which revealed a particular shortage in the Commonwealth of scientific workers in such fields as taxonomy, genetics and microbiology, completed the proceedings.

Textile Industry and the University of Leeds

THE report to the Clothworkers' Company of the Advisory Committee on the Departments of Textile Industries and Colour Chemistry and Dyeing, University of Leeds, 1945–46, pays a high tribute to the work of the late Prof. F. M. Rowe. No appointment has yet been made to the research fellowships in dyeing or in physical chemistry; but research workers of the Sisal Growers' Association have continued to be accommodated in the Dyeing Department. Dr. E. Race, in collaboration with Prof. Rowe and Prof. J. B. Speakman, established a new

technique for examining the constitution of the dye-chromium complexes obtained when wool is dyed with chrome mordant dyes, and with Dr. C. B. Stevens commenced work on the kinetics of chromium dye complex formation, including a study of the rates of formation and heats of combustion of chromium complexes of a series of dyes. Dr. E. M. Hunt and Prof. F. M. Rowe completed an investigation to establish degradation processes for determining the constitution of indigoid, thioindigoid and related types of vat dyes in substance, and Mr. F. M. Smith commenced a similar investigation of triphenylmethane dyes. Derivatives of catechol have been prepared for examination as intermediates for dyes, and Dr. A. T. Peters has completed an investigation of derivatives of 3 : 4-di-*tert.*-butylacenaphthene and derived indigoid dyes, and with Dr. R. J. Moualim commenced the preparation and orientation of a series of derivatives of 2-*tert.*-butylnaphthalene. Although the entry of British students was seriously affected by the demands of national service, the total number was fully maintained by ex-Service students and students from abroad, and the number of students in the Department of Textile Industries caused serious overcrowding.

The report of the latter Department refers to Prof. W. T. Astbury's election to the newly instituted chair of biomolecular structure, and when his work is transferred to new quarters, the Textile Physics Laboratories will be supervised by Mr. H. J. Woods, who has now been appointed lecturer in textile physics. A new scheme of work on textile finishing has been undertaken by Dr. C. S. Whewell in conjunction with Mr. C. R. Ricketts, and work on wool, rayon, jute and sisal has continued. Messrs. Courtaulds, Ltd., have now made a grant of £60,000 for building and equipping a Division of Rayon Technology within the Department. Lists of publications are included in the report.

Mosquitoes and Yellow Fever in the Sudan

Dr. J. Lewis, of the Stack Medical Research Laboratories, has discussed the relationship of mosquitoes and yellow fever in the Sudan (*Bull. Ent. Res.*, **3**, pt. 4; 1947). It appears that most of the southern half of the Sudan is a yellow fever area in the sense that people immune to the disease have been found in many parts of that territory. The chance of the disease spreading to parts hitherto free is liable to be increased by such outbreaks as the great Nuba Mountains epidemic of 1941. It is noteworthy that several towns in the Sudan lie on important air, rail and water routes leading to countries free from yellow fever. Some 140 species of mosquitoes are known from the Sudan, and, of these, twelve kinds are known to be capable of transmitting the yellow fever virus, while several other kinds are suspected in this connexion. Two further species are able to retain this virus throughout life without apparently possessing the ability to transmit the disease by their blood-sucking habits. The object of the present paper is to record information on the occurrence and distribution of mosquitoes in the Sudan. The Anophelines are only briefly considered because they are unlikely to transmit yellow fever. Among the Culicines that affect man and frequent human habitations, *Aedes taylori* is believed to be one of the chief vectors in the case of the Nuba Mountains epidemic. As regards *Aedes ægypti*, it appears that mosquito control measures have had the effect of rendering urban yellow fever epidemics, carried by this species, virtually impossible, and the disease has been exterminated from Khartoum. The relation of *Tæniorhynchus africanus* to the disease is of special interest owing to its wide range and abundance in the Sudan. While there is no evidence that this species can act as a vector, it seems likely that it can act in this way in limited epidemics about the Upper Nile area. The author concludes by discussing the measures of mosquito control in the Sudan, which greatly restrict the possibilities of the spread of yellow fever. At the same time it is evident that the control of a rural epidemic would be difficult to achieve.

University of London Appointments

The following appointments have been announced by the University of London: Mr. E. H. Phelps Brown, University lecturer in economics at Oxford, to the University chair of economics of labour tenable at the London School of Economics as from October 1; Dr. Harold Burton, senior lecturer in organic chemistry at the University of Leeds, to the University chair of chemistry tenable at King's College of Household and Social Science as from October 1; Mr. P. T. Bauer, lecturer in economics at the London School of Economics and Political Science, to the University readership in agricultural economics tenable at the School, as from October 1; Mr. R. H. Coase, lecturer in economics at the London School of Economics and Political Science since 1938, to the University readership in economics tenable at the School as from October 1; Dr. P. C. C. Garnham, senior parasitologist in charge of the Division of Insect-borne Diseases in the East African Medical Service, to the University readership in medical parasitology tenable at the London School of Hygiene and Tropical Medicine; Mr. J. W. H. King, senior lecturer in civil engineering at University College, Nottingham, to the University readership in civil engineering tenable at Queen Mary College as from October 1. Dr. M. M. Loève, lecturer at Birkbeck College, to the University readership in applied mathematics tenable at Birkbeck College as from October 1; Dr. F. T. G. Prunty, lecturer in chemical pathology at St. Thomas's Hospital Medical School, to the University readership in chemical pathology tenable at the School as from October 1; Dr. Richard Rado, lecturer in mathematics in the University of Sheffield, to the University readership in pure mathematics tenable at King's College as from October 1; Dr. F. R. Selbie, assistant pathologist at the Bland-Sutton Institute of Pathology, to the University readership in bacteriology tenable at Middlesex Hospital Medical School as from October 1.

The title of professor of zoology in the University has been conferred on Dr. Alastair Graham, in respect of the post held by him at Birkbeck College; the title of professor of zoology in the University has been conferred on Dr. A. J. Grove, in respect of the post held by him at Queen Mary College; the title of reader in pure mathematics in the University has been conferred on Dr. R. G. Cooke, in respect of the post held by him at Birkbeck College; the title of reader in civil engineering in the University has been conferred on Dr. S. R. Sparkes, in respect of the post held by him at the Imperial College of Science and Technology.

The degree of doctor of science has been conferred on Prof. E. J. King, professor of pathological chemistry at the Postgraduate Medical School.

LETTERS TO THE EDITORS

The Editors do not hold themselves responsible for opinions expressed by their correspondents. No notice is taken of anonymous communications

Elementary Isotopic Analysis : Determination of Nitrogen

We have recently described an isotopic method for the determination of oxygen[1] and carbon[2] in organic compounds by using heavy oxygen (O^{18}) and carbon (C^{13}) respectively in conjunction with a mass spectrometer. Using the same method, higher precision is possible in the determination of nitrogen and hydrogen, since N^{15} and H^2 (deuterium) are available in higher concentrations (30–35 per cent for N^{15}) than the oxygen isotope (1·2 per cent) and the carbon isotope (10–20 per cent).

In order to extend this method to nitrogen, we have made the following four determinations. Representatives of two types of compounds, heterocyclic and nitro, were chosen in view of the well-known difficulties of analysing them by the standard Kjeldahl method. The compounds used were pyridine ($n^{D}_{20} = 1{\cdot}5090$) and nitroethane ($n^{D}_{20} = 1{\cdot}3912$).

A known weight of substance (a) was burned simultaneously with a known weight (b) of pure isotopic $N^{15}H_3$ in a quartz tube, in the presence of an excess of copper oxide, copper and platinum wire, for 45–60 minutes. (Copper and platinum were inserted, of course, to reduce and equilibrate any oxides of nitrogen.) Both the pyridine and the nitroethane were burned at 750° C. The percentage of nitrogen (x) was calculated from our usual formula : $x = 100\,b(m - n)/an$, where m and n are, respectively, the initial and the final percentage excess of N^{15} in the ammonia and nitrogen.

Any air leakage into the sample, either during the run or during analysis, can be corrected for by calculating the air nitrogen contribution from the argon (mass = 40) peak. In a good determination the air nitrogen should be less than 3 per cent of the total nitrogen.

The results obtained are as follows :

Analysis	Pyridine, C_5H_5N 1	2	Nitroethane, $C_2H_5.NO_2$ 3	4
a, mgm. substance	25·56	30·02	25·04	16·97
b, mgm. N_2, added as NH_4Cl (using normal at. wt. of $N = 14{\cdot}008$)	1·79$_2$	4·27	4·43	3·43
m, % excess of N^{15} above normal (= 0·76%) in b	34·84	34·84	32·10	32·10
N^{15} content of equilibrium mixture (%)	10·52 10·59	16·30 16·18	16·50 16·38 16·34	17·55 17·54 17·47 17·43 17·56
	10·55±0·04	16·24±0·13	16·41±0·06	17·51±0·05
Average n, average % excess of N^{15} in equilibrium mixture	9·79	15·48	15·65	16·76
% N in substance, experimental	17·90±0·09	17·79±0·26	18·60±0·14	18·52±0·13
% N, theoretical	17·74	17·74	18·66	18·66

The mean probable deviation from the theoretical value is 0·4 per cent of the nitrogen content ; it is within the accuracy and precision of the Consolidated Engineering Corporation's mass spectrograph that we used.

A detailed description of our experiments will be published later.

Difficulties are encountered in the determination of *hydrogen* by this method because of wide differences in the rates of diffusion of protium and deuterium. Additional precise calibrations or changes in the construction of the present mass spectrographs would be necessary before our method can be successfully applied.

We are indebted to Dr. D. Rittenberg of Columbia University for the sample of $N^{15}H_3$ used.

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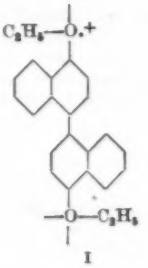
April 9.

[1] Grosse, A. V., Hindin, S. G., and Kirshenbaum, A. D., *J. Amer. Chem. Soc.*, **68**, 2119 (1946).
[2] Grosse, A. V., Kirshenbaum, A. D., and Hindin, S. G., *Science*, **105**, 101 (1947).

A Semi-Quinonoid Oxidation Product of 4 : 4-Diethoxydinaphthyl

The communication from Messrs. Hughes, Hush and Mellor[1] reporting a green oxidation product of tetramethyl-benzidine and the projected extension of work to related compounds renders desirable some account of our own work on the green colour instantly developed when 4 : 4′-diethoxydinaphthyl is dissolved in a large excess of concentrated sulphuric acid. The increase of intensity of absorption (measured at 660 mμ) is linear with that of concentration of the dinaphthyl until this reaches *c.* 310 mgm./litre. The solubility of oxygen in sulphuric acid being 33 mgm./litre[2], calculation shows the green colour to arise from the action of *c.* 8 gm. oxygen per gm. mol. diethoxydinaphthyl. A similar result follows if selenium dioxide or nitrous acid be used to intensify the colour. We therefore attribute the structure I to the green product.

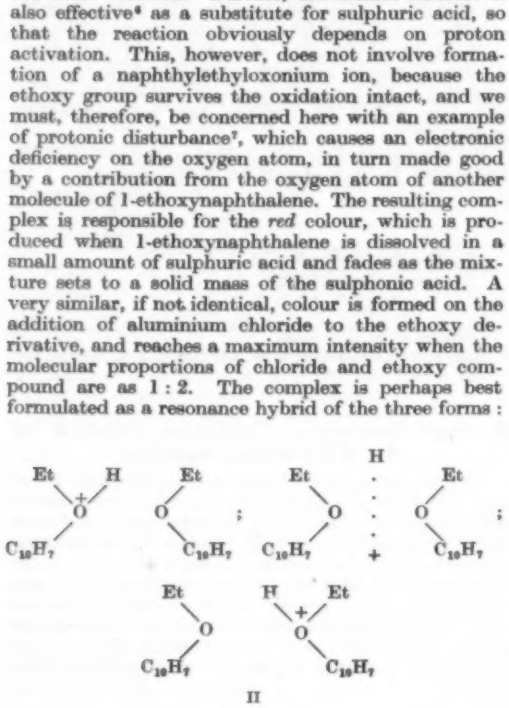


I

We expect to find that the blue, green and red colours developed by oxidation of diphenol[3], 3 : 3′-dimethyl-4 : 4′-dinaphthol[4], and dianthranol[5] respectively are of the same semi-quinonoid character and will develop in excess of sulphuric acid without further addition of an oxidizing agent.

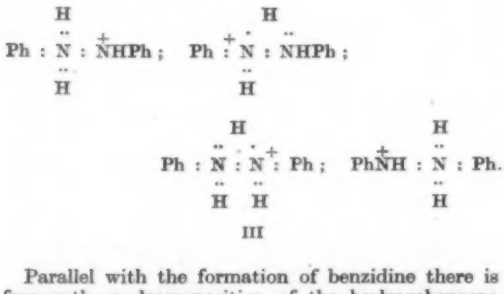
So far we have been less concerned with isolation of the semiquinonoid product (I) than with the general significance of the facts that : (1) the green colour is destroyed on addition of 1-ethoxynaphthalene, which is itself then converted to 4 : 4′-diethoxydinaphthyl ; (2) 1-ethoxynaphthalene itself causes

the development of the same green colouring matter in excess of sulphuric acid, but in this case only gradually. Nitric acid, aliphatic and aromatic nitro-compounds, bromine and selenium dioxide all promote the same reaction. Further, aluminium chloride is also effective[6] as a substitute for sulphuric acid, so that the reaction obviously depends on proton activation. This, however, does not involve formation of a naphthylethyloxonium ion, because the ethoxy group survives the oxidation intact, and we must, therefore, be concerned here with an example of protonic disturbance[7], which causes an electronic deficiency on the oxygen atom, in turn made good by a contribution from the oxygen atom of another molecule of 1-ethoxynaphthalene. The resulting complex is responsible for the *red* colour, which is produced when 1-ethoxynaphthalene is dissolved in a small amount of sulphuric acid and fades as the mixture sets to a solid mass of the sulphonic acid. A very similar, if not identical, colour is formed on the addition of aluminium chloride to the ethoxy derivative, and reaches a maximum intensity when the molecular proportions of chloride and ethoxy compound are as 1 : 2. The complex is perhaps best formulated as a resonance hybrid of the three forms :



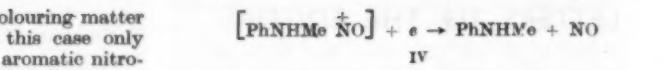
II

The stages by which this furnishes diethoxydinaphthyl are analogous to those by which the hydrazobenzene-proton complex (which we represent as the hybrid III) yields benzidine[8]. Indeed, Sir Robert Robinson has already adumbrated a connexion between the two types of reaction[9].

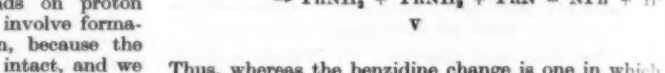


III

Parallel with the formation of benzidine there is frequently a decomposition of the hydrazobenzene to azo-derivative and amine. This reaction is specially favoured when the normal benzidine change is hindered or inhibited by 4 : 4′-disubstitution of the hydrazobenzene[9]. It appears not to have been realized that the reaction is exactly comparable with the oxidative splitting of the nitrosomethylaniline-proton complex studied by Jones and Kenner[5]. In more modern form, the correspondence between the two may be exhibited as follows :



IV



V

Thus, whereas the benzidine change is one in which electronic flow to one or other of the nitrogen atoms is intramolecular, it is intermolecular in the cases just mentioned. A complete description of the relevant proton-complexes in these instances would include, in addition to IV and V, radical forms as in II and III, and such forms were particularized by Jones and Kenner in their paper as operating "within the sphere of each other's action". Any discussion as to whether in this condition, which later was included in the conception of "the transition state", it is homolysis or heterolysis which occurs, is naturally devoid of significance.

Competitive reaction in promoting respectively exchange and substitution processes of proton or other kation, for example, nitronium ions, or nucleophilic reagents, with 1-ethoxy-naphthalene (or, indeed, any benzenoid compound) is, of course, subject to the usual regulative principles. Thus we find nitronium ion in concentrated sulphuric acid solution merely assisting the oxidative process already described as ensuing from proton attack, but very largely, if not exclusively, nitrating in 65 per cent sulphuric acid solution, in which protons are sufficiently diverted to hydroxonium ion formation, and the oxidative process does not occur. The observations of Martinsen[11] on the kinetics of nitration are also to be regarded in this manner rather than as attributable simply to the need for SO_4H' ions as acceptors of displaced protons[12].

Finally, this parallelism between the action of proton and nucleophilic reagents in substitution, coupled with the participation of radical forms in such complexes as II and III, supports the postulation of an analogous transition state, previously described by one of us and invoked to explain the formation of phenol[13] and other products, which frequently accompanies nitration. In fact, it is not too much to say that this general point of view pervades the above co-ordination of a wide range of phenomena.

A fuller account of this work, which will be extended, will be published in due course.

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May 9.

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[11] *Z. Phys. Chem.*, **50**, 385 (1905); **59**, 605 (1907).
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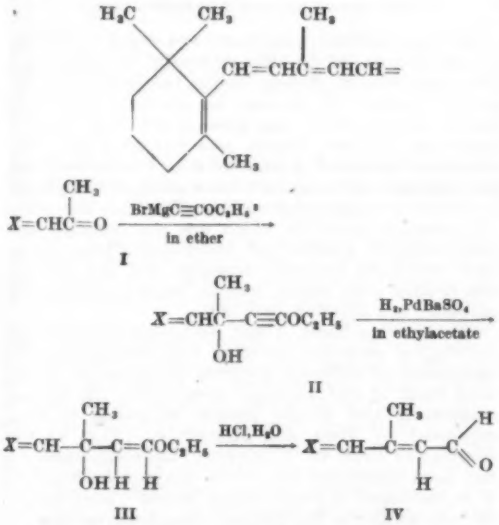
[13] Kenner, *Nature*, **156**, 369 (1945).

Synthesis of Vitamin A Aldehyde

In our communication in *Nature*, regarding the synthesis of vitamin A acid[1], we stated that "in the course of these investigations we received valuable assistance from Dr. H. H. Inhoffen, who suggested several other approaches to the problems". We have in the meantime learned that Dr. Inhoffen, who is now professor of organic chemistry in Brunswick, feels that the wording of this acknowledgment may give rise to misunderstanding. We therefore wish to point out that in the course of the occupation during the War, Dr. Inhoffen superintended and directed our work on the synthesis of vitamin A acid and vitamin A, and his advice was of great help in our work. When communications between Germany and the Netherlands were broken, joint publication could not be envisaged. We therefore had to single out that part of the work which we thought we could claim in good faith to be based mainly on our own ideas. This we have done to the best of our abilities. After our contact with Dr. Inhoffen ended in September 1944, we pursued the work along new lines and now present further results.

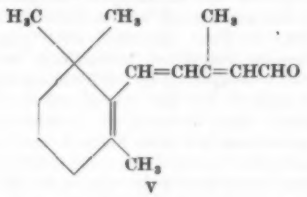
We have prepared vitamin A aldehyde from the C_{19} ketone I [1], as indicated in the following scheme. Writing *X* for



The aldehyde was characterized as its crystalline semicarbazone, m.p. 207–209° with decomposition. The absorption spectrum exhibits a well-defined maximum at 3750 A., log $E_{max} = 4{\cdot}87$. This corresponds with the absorption spectrum of the vitamin A aldehyde oxime[3] obtained by Hunter and Hawkins from natural vitamin A. With antimony trichloride in chloroform a very dilute solution of the semicarbazone in chloroform produces a purple-red colour; with a more concentrated solution the colour is blue-violet.

As the reduction of vitamin A aldehyde, obtained from natural vitamin A, has been previously described[4], a total synthesis of vitamin A now seems to be possible. We intend to synthesize vitamin A_2-aldehyde and vitamin A_2 according to the same scheme, starting from the C_{18}-ketone, derived from pseudo-ionone.

From β-ionone and ethoxyethynylmagnesium bromide we obtain, after an analogous series of reactions to those described above, β-ionylidene acetaldehyde V, identical in all respects with the substance described by Kuhn and Morris[5]. The absorption spectrum of the semicarbazone (m.p. 193–195°) had a single well-defined maximum at 3230 A.



V

With this substance we propose repeating the much discussed synthesis of vitamin A by Kuhn and Morris.

Our thanks are due to the Board of N. V. Organon for permission to publish this paper.

Note added in proof. In the meantime, we reduced the vitamin A aldehyde by means of aluminium-isopropoxide and isopropyl alcohol. After chromatography we obtained an oily fraction containing about 35 per cent of vitamin A according to its absorption spectrum and its biological activity. Further proof was obtained by conversion into anhydro vitamin A.

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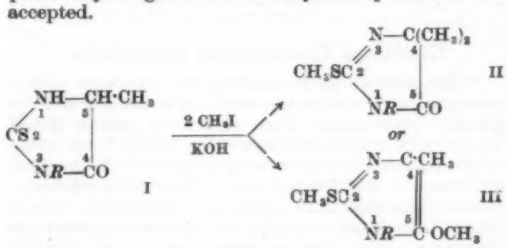
Reported Preparation of Mercaptoimidazole Derivatives by Methylation of 3 : 5-Disubstituted Thiohydantoins

In the examination of the ultra-violet absorption spectra of a number of methylated thiohydantoins, anomalous results were obtained if the structures previously assigned to the methylation products were accepted.



acid $\lambda_{max.}$ 2330 A.
$\epsilon_{max.}$ 20,000
alkali λ~ 2,360–2,420 A.
ϵ~ 4,500.
II, $R = CH_3$.

Thiohydantoins derived from alanine, for example, 2-thio-3 : 5-dimethylhydantoin (I, $R=CH_3$), methyl-

ate readily, two methyl groups being introduced into the molecule. Two products are possible (II and III), and Marckwald, Neumark and Stelzner[1] assigned structure III to the resulting derivative. Examination of the ultra-violet absorption spectra of the compound produced by the introduction of two methyl groups into 2-thio-3 : 5-dimethylhydantoin showed that this was unlikely to be correct. The spectra of this compound under differing conditions of *p*H were, in fact, identical with those shown under the same respective conditions by 1 : 4 : 4′-trimethyl-2-mercapto-5-ketodihydroimidazole (II, $R=CH_3$, prepared by the introduction of a single methyl group into 2-thio-3 : 5 : 5′-trimethylhydantoin). If structure III were correct, the conjugated double-bond system should show a spectrum markedly different from that shown by structure II.

Attention was then given to the compounds themselves. The methylated derivatives were bases, oily, and difficult to crystallize, and differing reports are available[2,3] of their properties and physical constants. Methylation products of a number of 2-thio-3-*R*-5-methylhydantoins and 2-thio-3-*R*-5 : 5′-dimethylhydantoins have now been prepared (*R* = methyl, phenyl and *o*-tolyl), and in each case the products of methylation from the two sources were found to be identical. As an example, the sulphate of 1 : 4 : 4′-trimethyl-2-mercapto-5-ketodihydroimidazole (prepared by monomethylation of 2-thio-3 : 5 : 5′-trimethylhydantoin) melted at 190–191° C.; the sulphate of the base produced by dimethylation of 2-thio-3 : 5-dimethylhydantoin also melted at 190–191° C., and there was no lowering in melting point on mixing the sulphates of the two bases.

It is obvious, therefore, that mercaptoimidazole derivatives (III) are not produced by dimethylation of 2-thio-3-*R*-5-methylhydantoins, the resulting products being 1-*R*-2-methylmercapto-4 : 4′-dimethyl-5-ketodihydroimidazoles (II).

A comprehensive account of this work will be submitted for publication at a later date.

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Chemical Constitution of Keratin

Wool fibres show histological structure when examined microscopically, and this structural heterogeneity has recently been shown in greater detail by the electron microscope[1,2,3]. Apart from some analyses on scale substance by Geiger[4], little chemical evidence on the composition of the different histological components is available. Recently, I have found that wool which has been deamidated by treatment with cetyl sulphonic acid[5] (0·05 *M*, 65°, 6½ days) will partially disperse if stirred in dilute alkali (*p*H *c.* 11, room temperature, overnight), leaving a suspension of the resistant residues of the scales and cortical cells. When the clear alkaline supernatant liquor is acidified to *p*H 4–5, a protein-like material is precipitated which is soluble in either dilute acid or alkali. A fairly complete amino-acid analysis of these components has been carried out and is given in the accompanying table together with data for the intact wool from which they were derived. *A* is the resistant component of the scales and cortical cells, *B* is the portion precipitated from the alkaline liquor, while *Aa* is the resistant residue from retreatment of part of *A* with cetyl sulphonic acid followed by dilute alkali. These analyses show quite clearly a great difference in amino-acid composition between *A* and *B* and the intact wool. The general tendency is for amino-acids of high molecular weight to be concentrated in the soluble component, while the resistant component is particularly rich in cystine and proline. The results thus show great similarities to those of Geiger[4], who probably analysed the resistant component of the scales.

Amino-acid composition of wool and components separated from it. (Nitrogen as % total nitrogen)

	Untreated wool	*A*	*Aa*	*B*
Total nitrogen	16·9	15·4	14·5	13·4*
Total sulphur	3·76	6·16	7·51	4·25*
Cystine	8·0	15·0	20·3	5·2
Phenylalanine	1·9	1·0	0·7	1·7
Leucine	6·7	5·3	3·6	9·2
Valine	3·6	3·9	3·5	4·0
Proline	3·8	6·7	7·6	1·0
Tyrosine	2·6	1·4	1·3	2·0
Alanine	3·2	4·2	3·3	4·0
Arginine	20·0	17·3	15·5	—
Hydroxamino-acids	12·8	14·0	—	—

* Not corrected for bound cetyl sulphonic acid.

Are these different components hydrolytic products of one keratin, or do they represent two keratins? The homogeneous protein insulin has been shown to give a cystine-rich fraction on enzymic digestion[6], and a similar effect has been noted with casein[7]. Moreover, Gordon, Martin and Synge[8] found that proline peptides of gelatin were especially resistant to hydrolysis, although in a later study of the partial hydrolysis products of gramicidin-S the only theoretically possible dipeptide which was not detected was prolyl-valine[9]. Fischer and Abderhalden[10] also found that prolonged enzymic digestion did not liberate free proline from casein, edestin, hæmoglobin, serum globulin, egg albumin or fibrin.

On the other hand, *A* and *Aa* possess recognizable histological structure pointing very strongly to the separation of different keratins pre-existent in the wool fibre. *A* and *Aa* may correspond to the fibrillar component and *B* the matrix substance of wool separated by Rees and Mercer[1,2,3]. Due to the courtesy of Prof. W. T. Astbury, the component *Aa* has been examined under the electron microscope. It is composed of fibrils which Mercer[11] considers to be very similar to the fibrillar component isolated by him. A possible mechanism for the separation of the two components by the present procedure is that deamidation of the matrix component renders it soluble in dilute alkali: a possible analogy for this is provided by the conversion of collagen to gelatin, which is also accompanied by a loss of amide-nitrogen.

If wool consists of more than one kind of keratin, the analytical data of the table throw grave doubt on any theory of wool structure based on correlations between X-ray data and chemical analyses of whole wool. Moreover, the occurrence of such a high percentage of proline residues in the fibrillar component suggests that Astbury's structure for keratin[12] requires modification to include the extensive folding of the chains which these residues cause[13,14]. The high proline and cystine content of the resistant components *A* and *Aa* may have special significance. For example, at least part of the (*C* + *D*) fraction[15]

of the combined cystine may owe its inertness to neighbouring proline residues, a suggestion which accords well with the previous hypothesis of the mode of linkage of this portion of the cystine[16].

An attempt to isolate cystine peptides from the $(C + D)$ fraction of the combined cystine of wool is now in progress, and together with full details of the work referred to will be published elsewhere.

Note added in proof. Preliminary qualitative examination of cystine peptides from the $(C + D)$ fraction of whole wool has confirmed the suggestion that proline is associated with this fraction. Glycine, alanine, serine and threonine seem also to be present in substantial amounts.

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May 6.

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Application of the Cathode Ray Oscillograph to Measurements of Short Life-Periods of Radioactive Sources

THE most accurate determinations of the life-periods of short-lived radioactive nuclei have been made using either coincidence circuits with variable resolving times[1], or the method of delayed coincidences[2].

Recent developments in cathode ray oscillographs have enabled measurements of this sort to be made in a more direct manner and with standard equipment. In this method, a pulse from one Geiger-Müller counter starts the single sweep on the oscillograph, and the output from a second counter is applied to the vertical plates. If these pulses are due to the radiations from a single radioactive source of short life, then observations on the distribution of the pulses seen on the screen enable an estimate of the half-life of the source to be made.

The method has been applied to the transformation

radium C $\xrightarrow{\beta}$ radium C′ $\xrightarrow{\alpha}$ radium D.

The β-ray from radium C is followed, after a short time-interval, by the emission of an α-ray from the daughter nucleus, radium C′. Observations on these time intervals enable the half-life of radium C′ to be estimated.

A thin-walled vessel containing radon gas was placed between two Geiger-Müller counters. One counter had a window of thickness sufficient to prevent α-particles and most of the β-particles from radium B being recorded. The other counter was operated in the proportional region so that it responded to α-particles only. The stopping power of the window of this counter was such that only radium C′ α-rays could penetrate.

The pulses from the counters were fed through suitable circuits to the oscilloscope, the β-counter initiating the sweep and the α-pulses being applied to the vertical deflexion plates. The instrument used was an Ultrascope, Mark 6, with three speed-ranges, namely, 25, 50 and 500 microsec. Incorporated in the time-base is a calibrating device consisting of an oscillatory circuit 'ringing' at a known frequency. The output of this causes the trace to be intersected by dark gaps representing known time-intervals. Hence visual observation of the pulses enabled their distribution in time to be recorded. Many of the pulses, of course, appear on the screen by chance, and it is necessary to perform control experiments in which the counters are irradiated by separate sources to allow for this.

The corrected distribution in time of the α-pulses shows an exponential fall giving a half-value period for radium C′ of 140 microsec. This result is not so accurate as that claimed for coincidence methods[1,2], but it is thought that the method is capable of being developed for the measurements of much shorter periods, in particular the life-time of metastable states which are of considerable interest theoretically.

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Constitution of Alkali Halide–Borate Glasses

Majumdar, Banerjee and Banerjee claim to have demonstrated[1] that sodium chloride dissolved in borax glass was present in the form of crystallites, and also that sodium chloride–boric oxide glasses gave the X-ray diffraction pattern of sodium chloride (together with some unidentified lines). The experimental work and deductions therefrom demand some comment and criticism.

There can be no objection to the experimental results obtained with the halide–borax glasses, since it has been shown that, in such systems as Na_2O—SiO_2 [2], Na_2O—B_2O_3 [3], there is an upper limit to the amount of alkali metal oxide which can exist in the vitreous phase. I have found the same type of phenomenon to occur with the systems CaO—B_2O_3, Na_2O—CaO—B_2O_3, RX—B_2O_3 (where R is Li, Na or K, and X is F, Cl, Br or I) and Na_2O—RX—B_2O_3. Thus a molten mixture of sodium carbonate and silica, in proportions to yield an $Na_2O : SiO_2$ ratio greater than that approximating to the metasilicate, $Na_2O.SiO_2$, separates into two phases on cooling. The crystalline phase, in a vitreous matrix, consists of impure sodium carbonate, probably a double salt of the carbonato-silicate type.

In binary borate systems, the limiting proportions for glass formation approximate to the compositions, for example, $Na_2O.2B_2O_3$ (that is, anhydrous borax), $NaF.2B_2O_3$ and $NaCl.3B_2O_3$. The precipitation of excess alkali compound is particularly well marked in the KF—B_2O_3 system, where a melt containing potassium fluoride, in excess of the limiting theoretical composition $3KF.2B_2O_3$, on cooling can produce very well-developed crystals of the halide up to 3 mm. in size.

The fact, therefore, that melts of borax and sodium chloride yield products which give the X-ray diffraction pattern of the alkali halide is not unexpected.

The glassy matrix itself, however, does not give a well-defined pattern, since it is a true glass, and the alkali halide in this vitreous phase is a part of the random structural arrangement. A complete discussion of the theory of the participation of fluorides and other compounds in the glass network will soon be published elsewhere. I wish, however, to dispute the general statement that alkali halides dissolved in glass are present as crystallites.

With regard to the halide–boric oxide systems, I have found no evidence for the presence of a crystalline phase except when, as stated above, the amount of halide was greater than the particular limiting composition of the system.

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Determination of Bilirubin in the Umbilical Blood as an Aid in the Early Diagnosis of Hæmolytic Disease in the Newborn

The bilirubin content of the blood is increased in hæmolytic conditions, as can be demonstrated by the indirect quantitative reaction of Van den Bergh. It seems probable, therefore, that the presence in the umbilical circulation of increased bilirubin, demonstrated by the indirect reaction, might be interpreted as early diagnostic evidence of hæmolytic disease of the newborn.

The bilirubin content of fœtal blood is not dependent on bilirubin of maternal origin, since bilirubin does not pass through the placental barrier[1]. The determination of the normal range of bilirubin in umbilical blood at birth is, however, extremely difficult, since this value varies widely and the fluctuations are associated with a series of factors[2].

In a series of 119 quantitative determinations of bilirubin in the umbilical blood by Van den Bergh's indirect method, we found values varying from traces to 3·6 mgm. per cent. Included in this series were only such cases in which both mother and fœtus were either *Rh*-positive or *Rh*-negative. In 42 of these cases, mother and fœtus had incompatible blood groups, so that immunization of the mother by fœtal erythrocytes was possible (for example, mother in group *A* and fœtus in group *B*, etc.). In this group of cases, 12 (28·5 per cent) had more than 2 mgm. per cent bilirubin in the umbilical blood.

In the remaining 77 cases, the mother and fœtus belonged to the same or to different but compatible blood groups (mother and fœtus both in group *A*, or mother in group *A* and fœtus in group *C*, etc.). In this group bilirubin in the umbilical blood exceeded 2 mgm. per cent in 9 cases (11·6 per cent).

A detailed report on the relationship between the bilirubin value in umbilical blood and the titre of maternal blood antibodies against fœtal erythrocytes will be reported elsewhere.

In 9 additional cases, the mothers were found to be *Rh*-negative, while their fœtuses were *Rh*-positive. In these cases there were from 0·8 to 2·4 mgm. per cent bilirubin in the umbilical blood. Congenital hæmolytic diseases of the newborn did not develop in any of them.

On the other hand, in three cases of *Rh*-negative mothers (two of whom had previously delivered at least one erythroblastotic fœtus) the bilirubin-levels in the umbilical blood were respectively 4·9, 8·1 and 6·2 mgm. per cent. Although the low titre of *Rh* antibodies (agglutinating, blocking and conglutinating) found in the maternal serum in these three cases seemed to indicate that no intensive immunization had taken place, all three newborn infants developed severe hæmolytic disease within 2–36 hours after delivery. Two of them, in whom the bilirubin values in the umbilical blood were 6·2 and 8·1 mgm. per cent respectively, died 38 and 96 hours after delivery. In the first case, the blood count made shortly before death was: erythrocytes 5,160,000 and Hb—17 (Sahli); and at autopsy, kernicterus was found. In the second, the blood count revealed: erythrocytes 1,360,000, Hb—6½ (Sahli). In both, the diagnosis of erythroblastosis fœtalis was confirmed at autopsy. The third (4·9 mgm. per cent of bilirubin in the umbilical blood) recovered from a very severe anæmia after repeated transfusions of *Rh*-negative blood.

Since jaundice and anæmia severe enough to cause death shortly after delivery may develop in infants apparently normal at birth, and since the antibody titre of the maternal blood did not always serve as an indication of the hæmolytic process in the fœtus, we consider a high value of bilirubin in the umbilical blood to be an indication of hæmolytic disease of the newborn. The presence of high bilirubin in the umbilical blood may, therefore, permit the early diagnosis of erythroblastosis fœtalis (anæmia neonatorum, icterus gravis and kernicterus).

These observations are considered to be preliminary, and a more extensive study is in progress.

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Relative Activities of *l*- and *dl*-Thyroxine

We have compared the biological activities of *l*- and *dl*-thyroxine in rats receiving 4-methyl-2-thiouracil by determining the 'thyroxine requirement' as defined by Griesbach and Purves[1]. This method consists of finding the amount of thyroxine which will prevent the pituitary basophil changes, resulting from the thyroxine deficiency produced by the blockage of thyroxine synthesis by the methyl thiouracil. The thyroxine samples used were: (1) *l*-thyroxine presented by Dr. C. R. Harington, and prepared by the iodination of *l*-di-iodothyronine[2]; (2) *l*-thyroxine presented by Dr. E. P. Reineke, and prepared by acid hydrolysis of iodinated casein[3]; (3) *l*-thyroxine prepared in this laboratory from *l*-di-iodotyrosine by the method of Harington and Pitt Rivers[4]; (4) *dl*-thyroxine presented by Burroughs Wellcome and Co., and prepared by alkaline hydrolysis of thyroid substance.

The 'thyroxine requirement' of the rat was found to be 2·3 micrograms of *dl*-thyroxine per 100 gm. per day. The equivalent value for *l*-thyroxine was 1·5 micrograms per 100 gm. per day, the same value being obtained for all three samples within the error of estimation, which we judge to be ± 5 per cent.

This gives a ratio of activities $l : dl = 1{\cdot}5 : 1{\cdot}0$; a result in conflict with the ratio of 2 : 1 found by Reineke and Turner[5], who estimated the amount of thyroxine necessary to prevent thyroid-weight changes in the thiouracil-treated rat.

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Autoradiography of Single Cells

The use of radioactive isotopes or tracers in the study of fundamental biological and biochemical problems has grown enormously during the last few years, and is likely to become still more important as larger quantities of various radioactive elements are made available. Certain types of problem can be solved by the application of well-known electrical methods to bulk tissue; it is recognized, however, that in any given tissue, individual cells may be in very different states or stages of development. For this reason the cytologist, in particular, wishes to study single cells. It is of interest to inquire, therefore, to what extent, if any, the photographic method of autoradiography can be applied to small organisms and single cells. It is clear from the work of Hamilton[1] and others that this technique is useful for large sections of tissue, but many other factors have to be taken into account when considering its applicability to single cells.

These factors may be stated quite simply, so long as we are only concerned with the question of detection in a given time. The problem of resolving power does not arise until conditions for detection have been proved favourable. In this note we are chiefly concerned with detection, and our calculations are based on existing data for radiophosphorus, P^{32}.

(1) *Radiophosphorus Supply.* A typical supply has an activity of 12 millicuries for a mass of 3·8 mgm. of phosphorus *immediately after irradiation*. Since 12 millicuries represent $12 \times 3{\cdot}7 \times 10^7$ disintegrations/sec., and the decay constant of P^{32} is $5{\cdot}6 \times 10^{-7}$ sec.$^{-1}$, it can easily be shown that the ratio of atoms P^{32}/P^{31} is $1 : 10^5$.

(2) *Phosphorus Content of Tissue and its Activity.* Marshak[2] has given results for the uptake of radiophosphorus by lymphoma and liver cells of mice. Our calculations are based on the values of P^{32} uptake for lymphoma cells two days after injection, when the uptake for lymphoma nuclei was greatest. On the whole, the activities of liver cells were less than those of lymphoma.

For lymphoma cells the uptake was found to be 4 per cent of the injected dose per gm. of tissue. This corresponds to an uptake of P^{32} of 0·4 per cent by weight of the total phosphorus present in the cell. The activity of the radiophosphorus supply mentioned in (1) is one hundred times the activity of that used by Marshak[2]. Using Marshak's figures, and making allowance for this fact, it can be shown that the activity of 1 gm. of tissue is 40 μc.

Suppose now that a layer of tissue one cell thick is to be autoradiographed, and that the cell has a thickness of 10 μ: the volume of cells presented to 1 sq. mm. of a photographic plate is then 10^{-5} c.c. For an activity of 40 μC./c.c. (the density of tissue is approximately unity), the activity per sq. mm. of plate is 0·4 millimicrocurie (mμC.).

(3) *Detection.* Lindsay and Craig[3], who have carried out P^{32} uptake experiments on larvæ and obtained uptakes similar to those of Marshak, mention that for X-ray film an exposure equivalent to 50 mμC./mm.^{2} was required for 1 minute. This figure has been confirmed by us in experiments using Industrex Type *D* X-ray film (Kodak) on the detection of drops of radiophosphorus solution (1 mμC. was detected and gave blackening sufficient for microphotometer measurements in 50 min.). Thus, with X-ray film an activity of 0·4 mμC./mm.^{2} would require a 2-hour exposure.

While we are here chiefly concerned with the problem of detection, the question of resolution cannot entirely be avoided, since the choice of the photographic plate is one of the determining factors. Assuming the linear dimensions of the cell to be of the order of 10 μ, a resolving power of at least 100 lines per mm. is desirable. Such plates (for example, Kodak *B*5 and *B*10) have about 1/50 of the speed of Industrex X-ray film. On this basis, an activity of 0·4 mμC./mm.^{2} would require an exposure of 4 days. The activity of the phosphorus used by Marshak (*loc. cit.*) was 1/100 of this figure, and the exposure required would, therefore, be about 40 days.

In order to make the autoradiographic technique a practicable one, a safety factor of at least 10 should be introduced to allow for (*a*) the decay of the phosphorus activity during the period of exposure, and (*b*) a certain degree of contrast in the picture to show the required detail; this, however, depends on the variation of concentration of P^{32} throughout the cell.

(4) *Conclusion.* The autoradiography of single cells having activities equal to those obtained by previous authors in experiments on bulk tissue is clearly impossible. Similar experiments carried out with more active radiophosphorus having a ratio of $\frac{\text{No. of atoms of } P^{32}}{\text{No. of atoms of } P^{31}} = \frac{1}{10^5}$, however, and using reasonably fine-grain plates, seem to be just possible. Since the possibility could only be realized in exposures lasting a few days, it is unlikely that autoradiographic techniques can be used to study migration of radioactive isotopes in single cells.

Autoradiographs should, however, be obtainable after a few hours exposure if (*a*) uptakes can be increased above the figure of 0·4 per cent, possibly by a series of injections lasting several days, or (*b*) the concentration of P^{32} in the sample of active phosphorus can be increased. Any improvements in the speed of photographic plates which may arise would also improve the possibilities of carrying out such experiments. There are obvious difficulties in maintaining biological material in a suitable condition for the long periods suggested by our calculations; moreover, no account has been taken of the biological effects of the β-radiation. Chromosomal aberrations, such as breaks and fragmentation, can readily be produced in root-tips growing in nutrient solutions containing radiophosphorus (as Miss M. Preston has recently shown in this laboratory). There are doubtless other effects; there is little point in discussing the biological implications of an experi-

ment which on physical grounds is possible, but scarcely practicable at the present time.

I wish to thank Prof. J. T. Randall and Dr. M. H. F. Wilkins for valuable discussions.

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Osmophilic Granules in Chromatolytic Nerve Cells

W. A. Stotler demonstrated at the sixtieth annual meeting of the American Association of Anatomists osmophilic granules in chromatolytic nerve cells; an account of this has been published[1]. This interesting finding is in agreement with our observations during the past few years[2], that when using the Marchi reaction for degenerated fibres not only the degenerating myelin can be shown by the Swank–Davenport method, but also fine black granules in certain nerve cells.

Further experiments on this point strongly suggest that such a cell is one in which the metabolic processes are interfered with by cutting at some distant point its axon or its terminations. If this could be confirmed by other workers on the central nervous system, a valuable additional method of identifying interconnexions within the central nervous system would be available.

I illustrate my point by a photograph of several nerve cells of the lateral thalamic nucleus showing the black granules arranged in a ring-like formation around the cell nucleus. In this particular experiment, the motor cortex was removed on June 1, 1944, and the rabbit was killed on June 6, 1944; and in this instance the changes in the thalamus were shown after a short interval between the operation and death, while in other instances these changes could be seen even after a considerable period of time.

I should like to emphasize also that the large motor cells of cranial nerve nuclei contain after a certain interval of time chromophile granules after extensive cortical damage. This obviously cannot be explained by chromatolytic changes, and an explanation of this particular phenomenon has yet to be found.

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Introduction of a Beetle from Trinidad into Mauritius to Control *l'herbe Condé* (*Cordia macrostachya*)

In all periods of human history, inadvertently or deliberately, man has introduced plants or animals of one country into another. In some cases the consequence has been tragic, but in others his action has achieved the desired result. In the later Middle Ages the Arabs introduced into Europe many vegetables, some of which have become established; spinach, for example. In the sixteenth century the Portuguese introduced many plants and animals from the Old World to the New and *vice versa*. In modern times, however, these introductions have been for a different purpose, frequently described as 'biological control'; by which is meant that man can use a natural enemy of an organism to cause its destruction for him. But this method has not always been successful because not all the factors that are involved in such transfers from one place to another are known, and, perhaps, not all of them can be completely known. But so far as they can be known, they ought to be taken into consideration.

My attention has been directed to the fact that a batch of *Physonota alutacea* Boheman (Cassidinæ, Coleoptera) has been recently introduced into Mauritius; which, it is hoped, will eat *l'herbe Condé*—*Cordia macrostachya* Roem. and Schult.—to such an extent that its unimpeded propagation will be checked. It should be remembered that this plant itself has been accidentally introduced into Mauritius.

Physonota alutacea Boheman occurs in Mexico, Central America, Venezuela, Colombia and Ecuador. It has also been found in San Francisco, Trinidad and the Galapagos Isles.

Physonota and other related genera belong to the New World and do not occur in the Old World. The Old World genus which is equivalent to *Physonota* is *Aspidomorpha*, and this does not occur at all in the New World. *Physonota* and its allies correspond to *Aspidomorpha* and its allies in general structure and habits so remarkably that one cannot help feeling that they must have descended from a common ancestor. From this relationship I assume that whatever food habits one group may have the other group probably will have.

The cassidine beetles have been known to eat plants of 26 out of 320 families as shown in the tables of my book (not yet published); the greatest number occurring on the Convolvulaceæ and the Compositæ. The beetles of the genus *Physonota* actually eat the following plants—Compositæ: *Helianthus* (sunflower), *Sonchus* (sowthistle); Boraginaceæ: *Cordia macrostachya*. In addition to *Physonota*, other New World cassidine beetles (*Coptocycla adamantica* Germer and *Cistudinella obducta* Boheman) have also been found on *Cordia*. It is important to remember this, since it means that if one species shows a taste for *Cordia* there are others which will have the same taste.

In the Convolvulaceæ the genera most attacked by cassidine beetles are *Convolvulus* and *Ipomœa* (sweet potato), and both Old and New World species of the Cassidinæ have been found on them. Therefore, although *Physonota* has not been actually found on the plants of these two genera, it is quite probable that *Physonota* will eat them.

The Old World genus *Aspidomorpha* occurs on *Argyreia* and *Quamoclit*—two genera also of the Con-

volvulaceæ. Three species of *Chelymorpha*, a New World genus allied to *Physonota*, have been found on three species of *Solanum* (Solanaceæ), including the potato. Three species belonging to two other genera of the New World have also been known to eat plants of *Solanum*. It seems likely, therefore, that *Physonota*, too, may feed on *Ipomœa* and *Solanum* as well as on *Cordia*.

Among the Gramineæ, both *Zea Mays* and *Saccharum* (sugar-cane) are attacked by *Chelymorpha*, the former also by a species of *Cassida*, a genus occurring in both New and Old Worlds; *Chirida*, another New World cassidine genus, also feeds on sugar-cane.

It is important to note that *Chelymorpha*, closely related to *Physonota*, has at least one species which is capable of eating the sugar-cane plant, and it is in the sugar-cane plantations that *Cordia* has become a nuisance. It is hoped that the introduced *Physonota* will behave as it is expected to do; but warning should be given that it may take a liking to sugar-cane, and even to the potato and sweet potato.

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Record of an African Fodder Grass from Central Burma

A number of exotic plants occur in the dry zone of central Burma. The annual rainfall of this area is only 25–35 in. in one monsoon, and the general vegetation is predominantly xerophytic—such as thorny shrubs, succulent species of *Euphorbia* and ephemerals. Some of these foreign plants are so well established that they could easily be mistaken for indigenous plants.

One of the common grasses of this dry zone is a scandent drought-resistant fodder grass, usually found trailing over thorny shrubs and common in hedgerows. This grass was sent to Kew in 1942, and has been identified by Mr. C. E. Hubbard as *Urochloa mosambicensis* (Hackel) Dandy[1]—a native of Central and East Africa. Other synonyms by which this grass is known are *Panicum mosambicense* Hackel[2], *Panicum notabile* Hook.f.[3] and *Echinochloa notabile* (Hook.f.) Rhind[4]. Both Hook.f. and Rhind expressed their doubts as to its affinities under the genera *Panicum* and *Echinochloa*, and Rhind contrasted its xerophytic characters with other species of *Echinochloa* of Burma.

On account of its value and possibilities as a fodder, this grass has attracted attention in Africa and Burma independently. It has been also introduced in Australia (Queensland), where it is said to be thriving well. It must have reached Burma very early, as Wallich collected it near the oilfields around Yenangyang in 1826 (Wall. Cat. 8723). Intentional introduction before Wallich's time is extremely unlikely, as traffic between the coasts of East Africa and Burma in those days was always scanty. Nevertheless, this appears to be the only possible route, as the plant is not recorded so far either from India or Malaysia. It is also not known how the plant reached Central Burma from the port (Rangoon), traversing the belt of heavy rainfall and swampy areas quite unsuitable for its growth. Most probably this took place accidentally, and the seeds must have been carried by river boats up the Irrawadi to the dry areas of central Burma, where the plant established itself.

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Errors of Estimation in Inverse Sampling

If a random sample of N individuals is taken from a population in which a proportion $P(= 1 - Q)$ possess a certain attribute, and of these N are found to possess the attribute, then, as is well known,

$$p = a/N$$

is an efficient and unbiased estimate of P. The variance of p is PQ/N; but unless N is large neither this quantity nor an estimate of it can be used directly in order to assign fiducial limits to p. If a probability level, say 0·05, is selected, upper and lower fiducial limits, p_U and p_L, may be defined; these are such that if P were equal to p_U, the probability of obtaining a or less individuals with the attribute in a sample of N would be 0·025, and if P were equal to p_L, the probability of obtaining a or more in a sample of N would be 0·025. Evaluation of p_U and p_L by successive approximation and summation of terms of a binomial expansion is tedious, but a table by W. L. Stevens[1] enables these 'true' limits to be obtained rapidly with sufficient accuracy for most practical purposes.

An alternative method of estimating P, that of *inverse sampling*, has been suggested as possessing advantages in some circumstances. This consists in taking individuals at random until a specified quota, A, possessing the attribute has been obtained. If this requires a total sample of n, the estimate of P is

$$p = (A - 1)/(n - 1);$$

the variance of p is approximately

$$s_p^2 = p^2q/(A - 2),$$

but s_p cannot be used for assigning fiducial limits to p except in large samples.

It may not have been generally realized that methods and tables for determining true fiducial limits for direct sampling may be adapted very easily to inverse sampling. For if p_U is the upper limit to a value of p estimated from inverse sampling, by definition it is the value of P for which the probability of obtaining the quota, A, in n or more trials is 0·025; this is the same as the value of p which, in direct sampling, would give $(A - 1)$ or less with the attribute in a sample of predetermined size $(n - 1)$. So p_L, the lower limit, is the value of P which would give the quota in n trials or less with a probability of 0·025, and is therefore the same as the value of p which, in direct sampling, would give A or more with the attribute in a sample of n. Hence the rule may be stated: in inverse sampling, the upper fiducial limit is the same as the upper limit for a direct sample with $N = (n - 1)$, $a = (A - 1)$, and the lower fiducial limit is the same as the lower limit for a direct sample with $N = n$, $a = A$. Stevens' table, entered according to his rules with the appropriate values of N, a, will then give the fiducial limits.

Haldane[2,3] has pointed out that, when p is small, its standard error in inverse sampling is practically a constant proportion of p for any fixed value of A.

Hence, by choice of a suitable value of A, the proportional standard error may be selected in advance of the sampling, a requirement which cannot be satisfied in direct sampling. Stevens' table records the limiting values of Np. For a fixed a and a fixed probability level, these are nearly independent of p, particularly for p less than 0·2; consequently, if P is known to be small, for any specified A, inverse sampling will give a value to $(p_U - p_L)/p$ almost independent of p. Hence, by suitable choice of A, the magnitude of the fiducial range relative to the estimate p may be determined approximately in advance of the sampling.

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Application of the Method of Steepest Descents to X-Ray Structure Analysis

ALTHOUGH the Fourier method of synthesis has enjoyed a long and justified supremacy in the armoury of techniques for X-ray structure analysis, the time is rapidly approaching when its use will be limited by the complexity of the structures investigated. In the absence of any universally applicable method of obtaining phase angles, Fourier refinement can be applied only to those structures which are sufficiently simple for an accurate estimate of their parameters to be made. It is an unfortunate fact that the Fourier refinement process converges only if the trial parameters are reasonably close to the true ones, and the region of convergence is roughly that of the differential method[1].

Even when the general shape and disposition of the atoms in a molecule are known, it is often extremely difficult, using only trial and error or Patterson–Harker methods, to find the proper location of that molecule in the unit cell, and it is evident that a first step towards a unified treatment of structure analysis would be a means of treating such groupings as a whole. The methods of molecular transforms[2] cannot be regarded as a satisfactory solution to this problem since, as soon as the space-group symmetry becomes at all complicated, they become difficult or impossible to apply.

A third feature which would be desirable is some means of refining density distributions. This is particularly the case with biomolecular substances since, although in general it is impossible to make even a conjecture as to their detailed structure, it may be possible to form a reasonable estimate of their general shape[3].

The purpose of this note is to explain briefly the application of the method of steepest descents to the above problems. The detailed techniques have been worked out and will appear in full elsewhere, but sufficient detail will be given here to allow of the application of the method in its simplest form.

Suppose that a set of observed structure factors $F_0(h,k,l)$ is given, then a set of atomic co-ordinates is called a correct structure if:

(1) $R = \Sigma \| F_0 | - | F_c \|$ or $R_2 = \Sigma\ (F_0^2 - F_c^2)^2$ is a minimum.

(2) The structure is not impossible on stereochemical grounds.

It is possible that a structure, correct from this point of view, may not be unique. If this is the case, however, there is no means of telling which of several structures, having the same minimum value of R or R_2, is the real one. So that the point is one of philosophical interest only.

Suppose that a set of trial parameters x_{rj} ($r = 1,2,-N$; $j = 1,2,3$) is given, the problem is to vary them so as to minimize R_2 in the most rapid manner. Now the equation $R_2 = \text{const.}$ represents some surface in the $3N$ dimensional space defined by the x_{rj}. The method of steepest descents simply specifies a procedure for moving from this surface to another having a smaller value of R_2. Starting from the point x_{rj} on $R_2 = C_1$, move in the direction of the normal to this surface until R_2 stops decreasing. Having arrived at this point on some surface $R_2 = C_2$, repeat the procedure. Evidently (neglecting cols and other singularities discussed elsewhere) the process converges to a minimum value of R_2, and the co-ordinates of this minimum are the required atomic parameters.

The analytical expression for the change ε_{rj} in any co-ordinate x_{rj} is simply:

$$\varepsilon_{rj} = -[\Sigma_{rj}\ (\partial R_2/\partial x_{rj})^2] \,.\, (\partial R_2/\partial x_{rj}) / \Sigma_{rj,r'j'}\ (\partial^2 R_2/\partial x_{rj}\partial x_{r'j'}) \,.\, (\partial R_2/\partial x_{rj}) \,.\, (\partial R_2/\partial x_{r'j'}), \qquad (1)$$

the derivatives being easily determined from the expression for R_2 and the algebraic form of $F(h,k,l)$.

In the early stages of a refinement it is usually easier to use the expression:

$$\varepsilon_{rj} = -2R_2 \,.\, (\partial R_2/\partial x_{rj}) / \Sigma_{rj}\ (\partial R_2/\partial x_{rj})^2; \qquad (2)$$

this requires care, however, as it leads to incorrect results when the x_{rj} are near their optimum values. As a practical rule, (2) should be used until a point is reached at which R_2 increases.

Similar expressions apply to R; but in this case particular care has to be exercised owing to the discontinuous nature of the moduli.

Despite the unpleasant appearance of (1) and (2), the calculations are quite easy, and much shorter than those of the Fourier method. As an example, the method was applied to the oxalic acid data and, starting from a *random* set of 2 parameters, the correct values were derived in three refinements which took only two and a half hours.

Application to the case of a known molecular shape is also easy; here the co-ordinates in some fixed set of axes are evaluated, and the whole frame of reference is rotated and translated until R or R_2 is minimized. The variables in this case are (x_0,y_0,z_0)—the co-ordinates of the origin, and (η,λ,μ)—the angles of rotation. Other applications cover the case where the molecule consists of a number of known groups, each of which can be treated as rigid.

Another modification of the method enables the molecule to be defined as a series of densities at lattice points; these densities are then varied to give a minimum value of R or R_2.

It is interesting to note that the method of least squares is a special case of the steepest descent technique, and is derivable from the same basic analysis.

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[1] Booth, A. D., *Trans. Farad. Soc.*, **42**, 617 (1946).
[2] Wrinch, D., "Fourier Transforms and Structure Factors" (A.S.X.R.E.D., 1946).
[3] Perutz, M., *Nature*, **149**, 491 (1942).

Effect of Bending on Selenium Rectifier Disks

BENDING a selenium rectifier disk causes a temporary increase of the current flowing through it in both directions. The effect (discovered in December 1942) is especially pronounced in the reverse direction, where a momentary increase of the current intensity up to 300 per cent and more can be produced through bending by hand, while in the forward direction values exceeding 5–10 per cent have not been observed. With copper oxide rectifiers no trace of a similar effect could be detected. The following, mostly qualitative, observations were made on our own disks, in the reverse direction: (1) The bending causes an increase of the current, whether the selenium layer lies on the convex or on the concave side of the disk. (2) In general, the stronger the bending the greater the effect. (3) The increase of current is, at its maximum, a temporary one. After bending a disk with a constant force, the momentary increased current intensity diminishes in the first few seconds rapidly, then slowly, and reaches its end value after some minutes. The behaviour of the disk is then, within certain narrow limits, that of a biased system: an increase of the bending increases also the current and *vice versa*. (4) Temperature has a pronounced influence; at 40–50° C., the effect is essentially smaller, and it seems to disappear more rapidly than at room temperature. (5) The effect depends upon the applied voltage. While at small voltages (1–2 volts) no effect is observable, with increasing voltages it increases also rapidly and reaches a maximal value as high as 350 per cent at 15–20 volts with some disks.

Selenium is a typical semi-conductor, its conductivity being due to the faults of the crystalline structure and to the impurities contained in it. Some of these centres are dissociated (into electron holes and negative ions) already in the mechanically finished disks, before forming, and determine the electrical properties of the disk at room temperature and below 1-2 volts. Further ionization—or expressed with modern terminology, transition of electrons to a conductivity-level—can be effected: (*a*) with thermal, (*b*) with electrical, and (*c*) with electrical plus mechanical energy. Thermal ionization goes on with any increase of temperature in the whole selenium layer and causes the temperature coefficient of the conductivity in the forward direction to be positive. Processes (*b*) and (*c*), however, take place only in the blocking layer, where an electrical field strong enough can be produced, thus explaining (*b*) the decrease of reverse resistance with increasing voltages and the phenomenon of 'electrical forming', with respect to (*c*) the bending effect.

In brief, we ascribe the bending effect to the dissociation of the impurity centres under the simultaneous action of electrical field intensity and the shearing stresses, impressed on the selenium layer by the bending. This assumption, together with the phenomenon of plastic relaxation, explains all the observations enumerated above.

Those interested in the new effect are invited to write for free samples of rectifier disks to the address below.

P. SELÉNYI
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May 30.

Transformation of Trichromatic Distribution Curves

The purpose of this communication is to bring to attention a point which does not seem to be generally realized although it is quite simple to prove. If one of a set of three colour-matching stimuli is altered, *the distribution curve for that stimulus is not changed*, though one or both of the other two distribution curves is altered.

Consider a colorimeter in which white is matched by a mixture of one trichromatic unit each of three stimuli X, Y and Z. If some of the stimulus X is transferred from its own beam to the Y beam, we shall have a new primary G; but since the match with white is unaffected, one trichromatic unit each will be present in the new system of X, G and Z. Since one unit of G contains one unit of Y, and also some X, it follows that in matching any colour with a mixture of X, G and Z the same number of units of G will be required as of Y in a mixture of X, Y and Z. The amounts of Z required in the two systems will be the same, though the amounts of X will be different. Therefore, the spectral distribution curve of X will be altered but that of G will remain the same as that of Y.

Let $\bar{x}$, $\bar{y}$ and $\bar{z}$ be the spectral distribution coefficients of stimuli X, Y and Z, and $\bar{r}$, $\bar{g}$ and $\bar{b}$ those of a new set of stimuli, R, G and B, the trichromatic coefficients of which in the X, Y, Z system are u_1,v_1,w_1; u_2,v_2,w_2; u_3,v_3,w_3; where $u + v + w = 1$. Then where

$$\frac{\bar{x}}{\bar{x}+\bar{y}+\bar{z}} = u_1, \quad \frac{\bar{y}}{\bar{x}+\bar{y}+\bar{z}} = v_1 \text{ and } \frac{\bar{z}}{\bar{x}+\bar{y}+\bar{z}} = w_1,$$

the following relations must hold:

$$\frac{\bar{r}}{\bar{r}+\bar{g}+\bar{b}} = 1, \quad \frac{\bar{g}}{\bar{r}+\bar{g}+\bar{b}} = 0, \quad \frac{\bar{b}}{\bar{r}+\bar{g}+\bar{b}} = 0,$$

so that $\bar{g}$ and $\bar{b}$ must both be zero.

Similarly, if $\frac{\bar{x}}{u_2} = \frac{\bar{y}}{v_2} = \frac{\bar{z}}{w_2} = \bar{x} + \bar{y} + \bar{z}$, $\bar{r}$ and $\bar{b}$ must both be zero, etc.

If the same white-point is adopted in the two systems, then $\bar{r} = \bar{g} = \bar{b}$ when $\bar{x} = \bar{y} = \bar{z}$; hence we can derive the transformation equations:

$$\bar{r} = \frac{\begin{vmatrix} \bar{x} & \bar{y} & \bar{z} \\ u_2 & v_2 & w_2 \\ u_3 & v_3 & w_3 \end{vmatrix}}{\begin{vmatrix} 1 & 1 & 1 \\ u_2 & v_2 & w_2 \\ u_3 & v_3 & w_3 \end{vmatrix}}; \quad \bar{g} = \frac{\begin{vmatrix} u_1 & v_1 & w_1 \\ \bar{x} & \bar{y} & \bar{z} \\ u_3 & v_3 & w_3 \end{vmatrix}}{\begin{vmatrix} u_1 & v_1 & w_1 \\ 1 & 1 & 1 \\ u_3 & v_3 & w_3 \end{vmatrix}}; \quad \bar{b} = \frac{\begin{vmatrix} u_1 & v_1 & w_1 \\ u_2 & v_2 & w_2 \\ \bar{x} & \bar{y} & \bar{z} \end{vmatrix}}{\begin{vmatrix} u_1 & v_1 & w_1 \\ u_2 & v_2 & w_2 \\ 1 & 1 & 1 \end{vmatrix}}.$$

It will be seen that $\bar{r}$ is independent of u_1, v_1 and w_1; that is, of the position of R. If only one, say G of R, G and B, is different from X, Y and Z we have $u_1 = w_2 = 1$, $v_1 = w_1 = u_3 = v_3 = 0$, and the equations reduce to:

$$\bar{r} = \frac{v_2\bar{x} - u_2\bar{y}}{v_2 - u_2}; \quad \bar{g} = \bar{y}; \text{ and } \bar{b} = \frac{v\bar{z} - w_2\bar{y}}{v_2 - w_2}.$$

Moreover, if G is somewhere on the line XY, so that $w_2 = 0$ and $u_2 = 1 - v_2$, we have:

$$\bar{r} = \frac{v_2\bar{x} - (1-v_2)\bar{y}}{2v_2 - 1}; \quad \bar{g} = \bar{y}; \text{ and } \bar{b} = \bar{z}.$$

In other words, altering the green primary alters only the red and blue distribution curves, and if the

green is moved along the red-green line the red distribution curve alone is changed.

It is perhaps of interest to note further that if in the last equation $v_2 \to \infty$, then $\bar{r} \to \frac{\bar{x} + \bar{y}}{2}$.

I wish to thank Mr. E. W. H. Selwyn and Dr. W. D. Wright for helpful comments.

A. Marriage

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May 12.

Combination Tones

From time to time attention has been given to the objective reality of so-called 'combination tones' produced when two simple tones are sounded together. We have recently had an opportunity of investigating this experimentally, using a wave analyser of the degenerative type, employing an electronic circuit described by one of us[1]. The analyser has a high selectivity corrresponding to a Q value of about 100.

An approximately sinusoidal voltage at a frequency of 1,025 c./s. was superimposed on another approximately sinusoidal voltage of frequency 735 c./s., the r.m.s. amplitudes being 200 mV. in each case. Search was made for the difference frequency (290 c./s.) and the summation frequency (1,760 c./s.), and these were found to be practically non-existent. The strength of the 290 c./s. component was about 1 mV., and the summation frequency was too weak to be measured, although its presence was detected.

The analyser was designed to handle a total of 500 mV. (with the particular attenuator setting used in the experiment) with minimum distortion. Nevertheless, some slight distortion is to be expected which would give a rectifying effect and would probably account for the traces of combination tones which were observed.

The two input signals were simply added linearly, and quite different results would be expected if the amplitude of one tone were modulated at the frequency of the other.

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[1] *Engineer*, June 7, 1946.

Sublimation in Outdoor Air

In a previous communication[1], experiments were described on the sublimation of water vapour in a Wilson chamber. It was found that in clean air sublimation commences only at temperatures below $-41{\cdot}2° \pm 0{\cdot}05°$ C., whereas in outdoor air at Oxford this threshold temperature is 9° C. higher.

With the view of investigating conditions at cloud-level, the Air Ministry arranged for me to visit the Hochalpine Forschungsstation at Jungfraujoch, which is 11,680 ft. above sea-level.

During tests lasting three weeks (April 1947) the threshold temperature there was found to be $-41{\cdot}2° \pm 0{\cdot}05°$ C., with the exception of two days, on which it rose to $-38°$ C. The air at Jungfraujoch during these two days was exceptionally hazy. On April 13 (the first occasion) there was an anticyclonic inversion which had developed during the previous night. On the second occasion, April 27, there was an exceptionally strong wind with general instability of the air mass.

It thus appears that whatever sublimation nuclei are effective in the lower air are usually absent from air at the height of Jungfraujoch.

This work is published by permission of the Director of the Meteorological Office.

B. M. Cwilong

Clarendon Laboratory,
Oxford. June 4.

[1] *Nature*, **155**, 361 (1945).

Silicon Flame Bands

We have recently made a preliminary study of the visible spectrum of flames of hydrogen charged with silicon tetrachloride burning in air. In a Méker burner with restricted supply of air, grey-blue cones are developed, and spectrograms of these taken on a low-dispersion prism instrument show a number of bands, apparently degraded to the violet, in the range 4200–5700 A. The strongest head is at about 5240 A., and a tentative vibrational analysis gives $\omega'' \sim 750$, $\omega' \sim 1050$ and $\nu_e \sim 19{,}000$ cm.$^{-1}$.

The circumstances in which these bands are produced suggest that the emitter may be Si_2, and the provisional values of the constants given above do not conflict with this view; but unambiguous identification must await the results of a detailed study with instruments of higher dispersion. This work is in progress.

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R. F. Barrow

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May 20.

What is a Dialysate ?

The "Oxford Dictionary" defines 'dialysate' as that portion of a mixture that remains after dialysis, and quotes Attfield's "Text-book of Chemistry" (1885). The quotation shows that the part that fails to pass through the membrane is referred to. From the point of view of the lexicographer, this is perfectly satisfactory; there seems to have been no earlier use of the word in print. Graham, for example, although he coined the word 'dialyser' and gave a new meaning to the word 'dialysis' did not apparently use 'dialysate'.

Present-day usage does not agree with the "Oxford Dictionary". Nearly all the biochemists that I have consulted have understood by dialysate the more diffusible part of the system. At present, therefore, the word is ambiguous unless the context makes the meaning clear. Many authors and editors have not read Attfield, and some of those who have may question his authority in the matter. The popular meaning has probably been adopted because of the analogy with filtrate, distillate, sublimate, etc.; in each case the more mobile part of the system is referred to. The continuing existence of this analogy will make it difficult to get universal acceptance of the dictionary meaning of dialysate.

We are left with no word except colloid for the part of a system that is retained by the dialysis membrane. This is unfortunate, but it is better than ambiguity.

N. W. Pirie

Rothamsted Experimental Station,
Harpenden. June 12.

BRITISH SCIENTIFIC INSTRUMENT RESEARCH ASSOCIATION

OPENING OF NEW LABORATORIES

A NEW chapter in the history of the British Scientific Instrument Research Association commenced on July 10, when the new laboratories of the Association at "Sira", Southill, Elmstead Woods, Kent, were formally opened by the Minister of Supply, the Right Hon. John Wilmot. The Association, which was founded in 1918, has been for many years handicapped by its limited resources and facilities. At the time of the inauguration of the Association, it could not do more than adapt a house in Russell Square, London, to laboratory use, and the limited facilities which were established there compelled the Association to direct its activities into certain well-defined channels of restricted operation. These circumstances made it difficult to attempt to establish a membership representative of all scientific instrument interests, and in consequence the Association has in the past prosecuted researches which, although extremely valuable to the particular interests served, have not ranged over the total requirements of the industry. From the commencement of the rearmament programme, many firms not in membership with the Association extended the scope of their activities to an extent which brought them within the field of research covered by it, and in consequence the membership, which at that time included twenty-five instrument firms, rapidly increased to more than one hundred. At the conclusion of the War, the Council of the Association formulated a scheme of expansion to permit it to meet the research needs of the enlarged membership in an adequate manner. This scheme was approved by the Department of Scientific and Industrial Research, which offered very considerable practical support, and it has now come to fruition.

The enlarged Association consists of six Experimental Departments and an Information Department. The Association was fortunate in acquiring a mansion at Elmstead Woods, Kent, which, by reason of the number and size of its rooms, was admirably suited to the experimental purposes of a research association. The work of conversion has been completed, and the experimental activities of the Association have now been transferred to the new laboratories at Elmstead Woods, situated in five acres of grounds in very beautiful surroundings, where the conditions of working are almost ideal.

Optical Instrument Department. A predominant feature of the past activities of the British Scientific Instrument Research Association has been work on problems associated with optical instrument production. While the Optical Department now takes its place as one of several, the facilities for this branch of the work have, in fact, been increased. The space devoted to optical work at Russell Square is now occupied by the Computing Section of the Department; while in the new premises a general optical laboratory has been established, ample provision has been made for the work on graticules and allied problems, and room has been set aside for interferometers and other standard testing equipment. The work of the Department can now expand beyond that connected with the processes and the materials used in manufacture to the investigation of problems of the actual instruments and to the development of new types.

Chemistry Department. Chemical research plays no small part in the activities of the Association, and the importance of this branch of the work is reflected in the excellent chemical laboratories to be found at "Sira". The old ballroom has been converted into a spacious general laboratory which is very completely equipped. In addition, two smaller laboratories provide facilities for specialized researches. The making of experimental melts of technical glasses, which has always been a main feature of the work of the Association, will be continued in a new glass-founding shop set up in an outhouse formerly used as a domestic laundry.

Physics Department. Many of the investigations undertaken by the Association are best carried out in orthodox physical laboratories. Three of the new laboratories have been allocated to physics; one is a large general physical laboratory, another is devoted to work involving high vacua, while the third has been set aside for special independent research.

Electrical Instruments Department. The Association has for many years included among its membership some manufacturers of electrical instruments; but experimental work carried out on their behalf has been limited to such as could be covered by normal chemical and physical laboratory facilities. There is no more heartening aspect of the expansion of the Association than that it permits problems peculiarly associated with electrical instruments to be investigated with adequacy. New laboratories have been equipped bearing especially in mind the needs of the electrical instrument membership, and benefits should accrue to this class of member on a scale far larger than was possible in the old circumstances.

Electronics Department. Electronics have in recent years made a very considerable incursion into the field of instrument design. Laboratories have been established in the new premises, which are equipped in a manner most suitable to the carrying out of investigation of problems arising through the application of electronics to scientific instruments. Any work carried out in the past by the Association in this connexion has been prosecuted under conditions of improvisation. The new laboratories have been planned and equipped specifically to meet the requirements of this branch of the Association's work.

Mechanical Department. The investigation of mechanical problems has not in the past fallen within the purview of the Association, and in consequence there has existed a wide gap in the service it has been possible to render to the makers of mechanical instruments or, in respect of their mechanical problems, to instrument makers in general. It is therefore most appropriate that mechanical facilities have been provided under the new scheme. A mechanical laboratory equipped with modern machine tools has been established, drawing office facilities are now available, and a modern workshop is in process of completion.

Information Department. The first fruits of the scheme of expansion was the establishment of a comprehensive Information Department and Library, which remain at Russell Square. The work of abstraction from numerous technical journals, incorporated in the monthly *Bulletin*, the provision of information on a very wide range of subjects, the library facilities, with its lending arrangements, have already proved of great benefit to the membership and to the research staff of the Association.

Such is the present position of the Association, which is looking forward to achieving on behalf of the scientific instrument industry as a whole even

more beneficial results than those which in the past have been enjoyed by a restricted section of the industry. Every branch of instrument making is now effectively represented in the membership of the Association, and the opportunity exists for the influence of the Association to spread in many new directions. In his speech at a luncheon which followed the opening ceremony, the Minister of Supply remarked, "The instrument makers look to the Association for help in solving their problems and overcoming their difficulties. From what I have learned of the Association, they will get this help. The member-firms of the Association are supplied with a monthly *Bulletin* dealing with the latest results in research and development, and there is, in addition, a fund of technical information available in the excellent Library maintained by the Association. The achievements of the Association are far too many to enumerate; but I was interested to learn that nearly two hundred research reports have been issued by the Association, and these, I know, are of great interest to the manufacturers. The British Scientific Instrument Research Association is the oldest surviving research association connected with the Department of Scientific and Industrial Research, having been formed in 1918, when it had no more than nine members; to-day the membership exceeds one hundred. The Association's record is such that with the greatly increased facilities at Elmstead Woods it will be surprising if the present membership is not increased in the near future. The Association has already contributed greatly to the tools and instruments which have established the good name of British workmanship in the past, and I am sure it will maintain and even improve this reputation. . . . I would like to express the gratitude of the Government in general and of my own Ministry in particular for the great achievements of the Association in the past."

POLLUTION BY TRADE WASTES FROM FOOD INDUSTRIES

THE cause and effects of pollution by waste waters from food industries, and the prevention of this pollution, were discussed by Dr. B. A. Southgate and Dr. S. H. Jenkins at a joint meeting of the Food Group of the Society of Chemical Industry and the Midland Section of the Society held at Birmingham on May 23; Mr. T. Rendle presided.

Some waste waters contain directly toxic substances such as cyanides, phenols, and metallic compounds; in wastes from the food industries, however, pollution is due mainly to organic matter in solution and in suspension. Organic matter discharged into a stream is oxidized by bacterial action at the expense of the oxygen dissolved in the water. The rate of oxidation increases with rise in temperature; consequently a rise in temperature causes a decrease in the concentration of oxygen dissolved in the water, because this is the result of an equilibrium between the rate at which it is used in processes of oxidation and the rate at which it is absorbed from the atmosphere. As an illustration, in the winter the polluted estuary of the River Tees may contain dissolved oxygen equivalent to 70–80 per cent of the amount required to saturate the water, whereas in summer the corresponding concentration may be as little as 0 to 10 per cent of the saturation value. If the content of dissolved oxygen falls below about 50 per cent of the saturation value, the water may be unsuitable for fish, though they can live at much lower concentrations, particularly at low temperatures, at least for comparatively short periods.

Other effects of discharge of waste waters from the food industries include the deposition of organic sludge which may undergo anaerobic fermentation in warm weather, and which may cause marked changes in the distribution of bottom-living invertebrates, many of which serve as food for fish. Discharge of organic matter may also lead to the growth of 'sewage fungus'; this term is applied to a wide variety of Bacteria, Fungi, and Protozoa or associations of them, usually whitish-grey in colour and resembling cotton wool in appearance. These growths are found adhering to vegetation and stones in many polluted streams, and usually cause silting on the river bed. When the fungus dies it is decomposed by bacterial action, with absorption of oxygen from the water and sometimes with evolution of hydrogen sulphide.

Waste waters from food industries may cause difficulty in the use of surface waters for domestic supply; the presence of organic matter may make the water unpalatable; ammonia may interfere with the treatment of water by chlorination; and nitrogenous compounds may stimulate growth of Algæ which cause difficulty in sand filters and may also give rise to unpleasant tastes.

When the construction of a food factory is being planned, the possibility of pollution resulting from trade effluents must be borne in mind. Pollution is sometimes avoidable by erecting factories where sewers and sewage disposal works are at hand to deal with any waste water. When vegetables or fruit must be conveyed to a factory in a fresh condition, this is not always possible, and treatment of the waste water at the factory then becomes necessary.

The volume of waste water produced and its impurity content varies greatly from factory to factory, depending upon the product made, the management, and the amount of water available for processing. The organic matter in the waste water can be expressed in terms of an equivalent amount of domestic sewage and therefore in terms of population. For example, a beet sugar factory handling 1,000 tons of beet daily may discharge up to four million gallons of waste water daily, containing organic matter equivalent, in some cases, to the sewage from about 2,000 persons and in other cases to the sewage from 20,000 persons. Food wastes show marked fluctuations in the polluting matter content because processing varies with the time of year: a tenfold increase in the polluting strength of the waste water within a matter of a few weeks is not at all uncommon. This variation in strength, and also the fact that the waste water is frequently produced over a short period of the day, introduces difficulties in designing treatment plants for purifying the factory wastes.

The methods used for purifying food wastes have developed from those employed for sewage treatment. Fibrous matter, rootlets, peelings, etc., are removed by passing the water through screens; suspended mineral matter is then separated and the organic matter in suspension removed by continuous passage through sedimentation tanks. The residual polluting matter in solution is eliminated by biological oxidation by: (1) allowing the liquid to percolate through suitable soil; (2) distributing it over a filter bed made of inert material resting on a well-drained floor, so as to cultivate on the inert material a flora

and fauna able to oxidize the organic impurity in the waste water; or (3) aerating a mixture of the waste water and a heterogeneous culture, known as activated sludge, which consists of organisms grown from the waste water.

All pollution prevention authorities agree that industrial wastes are best treated at sewage purification works. The Public Health (Drainage of Trade Premises) Act, 1937, gives manufacturers the right to use public sewers and sewage works for disposing of trade wastes, provided they do not injure structural materials or inhibit purification. Some food wastes, especially those from the fermentation industries, may cause very serious interference with treatment of the sewage when present in high concentration, but ordinarily the difficulties encountered are surmountable.

In discussion of the two papers, it was stated that the growths in a river receiving beet sugar waste had caused trouble on the screens at an electric power station ten miles below the factory. Wastes containing sugar favour such growths over a long stretch of river in cold weather: in warm weather, the sugar is rapidly oxidized and so the region of pollution is smaller, though the extent of pollution is greater. Decomposition of solid matter on the bed of a stream was also discussed. Anaerobic organisms break down such matter into gaseous products, or into substances which are then oxidized by aerobic organisms. The effects of Algæ were also mentioned. During the day, photosynthesis by Algæ raises the dissolved oxygen concentration in rivers, and when algal growth is marked, there is a diurnal variation in the dissolved oxygen content of the water. A prolific growth of Algæ might be followed by a lowering of the dissolved oxygen in the water when the Algæ die and decompose.

Further discussion was concerned with methods of analysis, means for assessing the amount of polluting matter in waste water, the treatment of wastes by means of chemical precipitants, the disposal of the sludge or solid matter in waste water, the dissolved oxygen content of sea water, and the difficulty of obtaining supplies of constructional materials for trade-waste purification plant.

A NON-SPECIFIC RESISTANCE FACTOR IN THE ALBUMIN RESIDUE REVEALED BY THE SERIAL CEPHALIN FLOCCULATION CURVE

By Dr. JACK G. MAKARI
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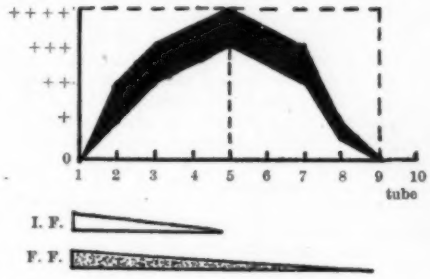
IN the last laboratory meeting of the Royal Society of Tropical Medicine, I demonstrated the various types of serial cephalin flocculation curves as obtained in health and disease with a special reference to their application in tropical derangements. In obtaining the curves, the serial dilution method was followed[1], using ten tubes instead of Hanger's original one-tube method[2]. Serial cephalin flocculation curve I, shown in the accompanying figure, represents the normal range in fifty healthy volunteers. In a study of the mechanism of Hanger's test, which is comparable to the first tube in the serial dilution method, Kabat, Hanger *et al.*[3] found the flocculating factor to be associated with the γ globulin. They failed, however, to find an inhibiting fraction in the albumins. Moore, Pierson *et al.*[4], two years later, reported from the same laboratory the presence of an inhibiting fraction associated with the albumins. It is to be noted that these workers were using electrophoresis by means of which albumins appear homogeneous[5]. Dennis and Makari[6], using salting-out methods, found the greatest concentrations of this inhibiting factor in the albumin residue. Since this inhibiting factor was found by the latter workers to be originally present in the serum in smaller amounts than the flocculating factor, the critical dilution-level of 0·04 mgm. is reached much earlier in the case of the inhibiting factor. The first zone representing the first five tubes in the figure presents, therefore, a delicate balance between flocculating factor (γ globulin) and inhibiting factor (albumin residue). In the second zone only the former is at work. This delicate balance in this first zone represents as well a balance between the liver and reticulo-endothelial system.



Further study of this inhibiting factor present in the albumin residue of man and revealed by the first zone of the serial cephalin flocculation curve shows that it plays an important part in relation to drug administration, immunization, relapse and the outcome of infection in man.

The figures in the tables indicate the extent of deviation of this inhibiting factor from the normal range in health (serial cephalin flocculation curve I) recorded in ⅛ in. square units. A deviation below the normal curve, that is, an increase in inhibition, is designated as positive, while a deviation in the opposite direction is designated as negative. Reference to the dosage is made as follows: for quinine up to 3 gm. as small dose, 3–6 gm. as medium dose, and more than 6 gm. as large dose; for atebrin up to 0·6 gm. as small dose, between 0·6 and 1·2 gm. as medium dose, and larger amounts than 1·2 gm. as large dose.

Vaccination with T.A.B. was accomplished by the subcutaneous administration of 500 million bacteria; a double dose was given one week later and repeated one week later still. The typhoid cases studied were reported earlier in relation to Hanger's test[7].

No reference is made in this preliminary report to changes in the flocculating factor which reflect reticulo-endothelial stimulation. This latter aspect will be referred to in the detailed report.

It is apparent from Table 1 that both quinine and atebrin give rise in healthy volunteers to a positive inhibiting factor response; atebrin resulting in greater stimulation over a shorter period.

A transient positive inhibiting factor response is also observed as a very early manifestation of

TABLE 1

	Treatment given	Deviation of I.F. response from normal S.C.F. curve I				
		Before treatment	After small dose	After medium dose	After large dose	Residual effect (1 week later)
Normal volunteers						
(a) Group I (average in 6)	Quinine	0	0	+11	+11	0
(b) Group II (average in 5)	Atebrin	0	0	0	+15	−1
Malaria, *P. vivax*						
(a) Primo infection						
1 Yahya (2nd day)	Quinine	+14	0	−5	−10	+5
2 Mansour (6th day)	Quinine	−10	−5	−4	−21	
	Atebrin			−10	+23	
3 Omaima (10th day)	Quinine	−5	−3	0		
(b) Relapsing malaria						
4 Mary (8th month)	Atebrin	−10	+5	−15	+9	0
5 Souad (18th month)	Atebrin	−18	−13	+14	+16	+32
Malaria, *P. falciparum*						
(a) With cerebral symptoms						
6 Hassib (4th week)	Atebrin	−24		−24	−24	
7 Samaha (4th week)	Atebrin	−24			−10	
(b) Without cerebral symptoms						
8 Paul (2nd week)	Atebrin	−4		−4	0	
9 Mohamed (2nd week)	Atebrin	−6	−2		−5	0
10 Farhan (4th week)	Atebrin	−4			−1	
(c) With blackwater fever						
11 Atassi	Atebrin	−21	−5		+16	0

TABLE 2

	Deviation of I.F. response from normal S.C.F. curve I										
	Before	1st week	2nd week	3rd week	4th week	5th week	6th week	7th week	8th week	8th month	12th month
Normal volunteers (average of 50) Effect of vaccination with T.A.B.	0	+9	+5						+1	0	0
Typhoid cases—uninoculated											
(a) Severe infection		−1	−4	−10	−10	−4	−1	−1	0		
(b) Moderately severe case with relapse		−4	+5	−10	−10	−4	0				
Typhoid cases—inoculated		−1	+10	+32							

malarial infection (Case 1). This soon gives way to a negative response, which was more marked in Case 2 observed on the sixth day of illness and less so in Case 3 observed on the tenth day of illness. More marked initial inhibiting factor depletion was obtained in the two cases of relapsing malaria and most marked in *P. falciparum* infections with cerebral manifestations (Cases 6 and 7), and with blackwater fever (Case 11).

The course of the struggle between the malarial parasite and the host as well as the aid provided by quinine and atebrin seem to be mirrored by fluctuations in this inhibiting factor response. Thus a renewal of clinical activity in Case 2 was ushered in by a maximal negative inhibiting factor depletion, while a positive inhibiting factor response was associated with a remission. A similar finding was observed in a typhoid relapse (Table 2).

Furthermore, the extent of these fluctuations and the degree of residual stimulation seems to be of significance in determining the outcome of this struggle. Thus in two cases of relapsing malaria, Case 4 showed more fluctuations but no residual inhibiting factor stimulation, while Case 5 showed a steady increase in inhibiting factor with a maximal residual inhibiting factor response. The former patient continued relapsing for another eight months, while the latter showed no more relapses over a two-year period of follow up. In the two cases of *P. falciparum* infections with cerebral manifestations, it was found that Case 6 showed a complete absence of any inhibiting factor response despite 2 gm. of atebrin, while Case 7 showed a sluggish response. The former died while in the hospital, and the latter left the hospital as improved.

Of interest is the very sluggish inhibiting factor response obtained despite atebrin therapy in all *P. falciparum* infections. The only exception encountered was the case of blackwater fever, which showed a surprisingly good inhibiting factor response, even to the small dose of atebrin given.

Table 2 shows the positive inhibiting factor response obtained in fifty healthy volunteers as a result of immunization with T.A.B. vaccine. It also shows the negative inhibiting factor response which results from infection with *E. typhi*. In a severe case observed in a non-inoculated patient this negative inhibiting factor response appeared in the first week, reached maximal depletion in the third week and remained until the eighth week. In contrast to that the phase of negative inhibiting factor response was much shorter in the inoculated group, being over by the second week. This was in agreement with the clinical severity observed in the uninoculated as compared to the inoculated groups.

There is therefore evidence to indicate that this inhibiting factor present in the albumin residue of man, which is detectable in the serial cephalin flocculation curve and which is possibly elaborated by the liver, is in fact a *resistance factor*—of great importance in determining the course and outcome of this struggle between host and parasite. A decrease of this resistance factor shifts the balance in favour of the parasite, while an increase shifts the balance in favour of the host.

Such an increase in the resistance factor could be brought about by two different mechanisms:

(1) An immediate and non-specific increase as a result of the administration of *non-antigenic* substances as in the case of the two drugs used, quinine

and atebrin. This effect is maximal during the administration of the drug, when large doses are reached. There seems to be no residual and no delayed effects.

(2) A residual and a delayed increase brought about by the repeated administration of *antigenic* substances as in the case of T.A.B. vaccine or as occurs with repeated attacks of malaria and the resultant liberation of malarial proteins. This second mechanism seems to be more specific, but is distinct from the specific globulin antibody response which is also obtained in these cases. The residual effect obtained in the case of this resistance factor was maximal one week after the cessation of immunization, whereas the antibody response demonstrated by the zone of flocculation in the serial cephalin flocculation curve was maximal two weeks after the cessation of immunization.

The delayed effect comes into action whenever the immunized host is infected with the same agent.

A more detailed account is in the press.

I wish to thank Prof. E. W. Dennis, head of the Department of Bacteriology and Parasitology of the American University of Beirut, for his valuable advice.

[1] Makari, J. G., *J. Trop. Med. and Hyg.*, **49**, 113 (1946).
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[3] Kabat, E. A., Hanger, F. M., Moore, D. H., and Landow, H., *J. Clin. Invest.*, **22**, 563 (1943).
[4] Moore, D. B., Pierson, P. S., Hanger, F. M., and Moore, D. H., *J. Clin Invest.*, **24**, 292 (1945).
[5] Cohn, E. J., Oneley, J. L., Strong, L. E., Armstrong, S. H., and Hughes, W. L., Jr., *J. Clin. Invest.*, **23**, 417 (1944).
[6] Dennis, E. W., and Makari, J. G., in the press.
[7] Makari, J. G., *J. Trop. Med. and Hyg.* **49**, 70 (1946).

INTERSTELLAR MATTER

THE George Darwin Lecture entitled "Some Phenomena connected with Interstellar Matter" was delivered by Prof. J. H. Oort before the Royal Astronomical Society on May 10, 1946, and the lecture has now been published in full (*Mon. Not. Roy. Astro. Soc.*, **106**, 3; 1946). Prof. Oort deals more with a survey of the problems presented by interstellar matter than with an account of our present knowledge on the subject. The uneven distribution of interstellar matter is the first characteristic that strikes the investigator, and this applies to interstellar gas as well as to obscuring clouds. On the average, the light from a star 1,000 parsecs distant traverses five clouds, and it can now be accepted that the dark clouds contain proportionate concentration of gas. It has been shown that, on the average, the intensities of interstellar lines increase proportionally with the distances of the stars in all galactic longitudes, the only explanation of which is that these lines are mainly formed in clouds having 'peculiar' velocities averaging 15 to 20 km./sec. in the radial component.

The very uneven distribution of obscuring matter is noticeable even in the galactic plane, and two extended systems of dark clouds are found in our neighbourhood, one in the Taurus–Auriga–Perseus region, and the other in Ophiuchus and Scorpius. Both systems cover regions of about 500 square degrees and show an average absorption of mag. 0·8, although they are comparatively close to us—about 100–150 parsecs. In contrast to the strong absorption in these clouds, there are very faint Cepheids in Cygnus the apparent magnitudes of which are scarcely affected by absorption, although their distances are between 10,000 and 20,000 parsecs. As the average diameters of the interstellar clouds are of the order 100 parsecs and their peculiar velocities 20 km./sec., a cloud will encounter another in about 10^7 years, and some remarkable effects will result from such an encounter. Incidentally, it might be expected that the individual cloud systems and their relative motions would disappear in a time short in comparison with the age of the galactic system; but as this has not occurred there must be some mechanism causing reformation and motion. Independent data suggest that this is taking place, and the six-colour photometry carried out by Stebbins and Whitford, as well as other evidence, show that the dependence of interstellar scattering upon wave-length is the same for all stars, no variation occurring whether observations are made through dense clouds or through a thin medium. This implies that particles within dense clouds have the same radii as outside particles; and if it is assumed that these particles grow by condensation from the interstellar gas, the only interpretation is that the clouds are being continually reshuffled.

Two effects will result from an encounter between clouds. First of all, the intermediate region between the clouds will be compressed, and if the relative velocity of an encounter is 30 km./sec., the density and temperature in this region will be three times their value in the clouds. Hydrogen will be ionized by collisions and the gas will become luminous, the luminosity being most conspicuous when the interface between the clouds is in the line of sight from the earth. This may be the explanation of the bright rings often observed near the dark nebulæ when these are bordered by luminous nebulæ, and the luminescence of nebulæ like the extensive nebulosities near Zeta Orionis or the North American nebula may be caused by this collisional mechanism rather than by radiation from the stars.

Another effect is the evaporation of the solid particles of the two colliding clouds when the particles of one cloud hit other particles of comparable size. The probability of such evaporation cannot be ignored, and it may play an important part in the realm of interstellar material. This leads to the problem of the origin and growth of these solid interstellar particles, of which the radii are 1,000 A. A full discussion of this last and very important question would be impossible in the limited space, but briefly it can be said that an order of magnitude of 10^{-24} gm./c.c. for the density should preserve a balance between condensation and evaporation.

Among other astronomical problems in which interstellar material plays an important part reference may be made to the significance of interstellar material in the extragalactic nebulæ. There is no trace of it in the elliptic nebulæ; but it is very prominent in the spiral nebulæ, especially in the case of objects seen on edge. If the dark matter were comparable in mass with all the stars in a nebula, it might lead to instability, and spiral arms would be formed. The absence of such material in the elliptic nebulæ would offer a possible explanation of their stability; but it is admitted that such suggestions are still merely speculative.

The problem of the resistance of interstellar gas to the expanding shell thrown off by a nova is considered, and it is shown that in the case of an ordinary nova expanding in an interstellar medium of average density the deceleration should be observable within half a century. For supernovæ the deceleration would become visible only after several thousand years.

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

SENIOR ASSISTANT to teach CIVIL ENGINEERING subjects, particularly Surveying and Structures to honours degree standard, ASSISTANT LECTURERS to teach in some selected branch of CIVIL or MECHANICAL ENGINEERING up to degree standard, ASSISTANT LECTURERS to teach classes of a WORKSHOP or PRODUCTION ENGINEERING character up to Higher National Certificate in Production Engineering and/or Motor Vehicle Service work for the National Craftsman's Certificate, and a LECTURER IN MATHEMATICS—The Clerk to the Governors, Woolwich Polytechnic, Woolwich, London, S.E.18 (August 16).

LECTURER IN METALLURGY with Special Responsibility—The Principal, Central Technical College, Suffolk Street, Birmingham 1 (August 16).

LECTURER (Grade I) IN ORGANIC CHEMISTRY, a LECTURER (Grade IIa) IN CHEMISTRY, and LECTURERS (2, one Grade I, one Grade IIc), mainly for research into the chemistry of high polymers and elastomers—The Secretary, The University, Edmund Street, Birmingham 3 (August 18).

BIOCHEMIST for research in endocrinological unit—Prof. Zuckerman, Anatomy Department, Medical School, Hospitals Centre, Birmingham 15 (August 18).

PHYSICIST for research on applications of physics to medical problems, and an ASSISTANT PHYSICIST—The Secretary, Barnato Joel Laboratories, Middlesex Hospital, London, W.1 (August 23).

ZOOLOGIST for work in collaboration with the Water Pollution Research Laboratory at Watford on ecological and physiological problems connected with polluted waters—The Director, Freshwater Biological Association, Wray Castle, Ambleside, Westmorland (August 23).

LECTURER (Grade II) IN MECHANICAL ENGINEERING, and ASSISTANT LECTURERS (Grade III) IN THE MECHANICAL ENGINEERING AND CIVIL ENGINEERING DEPARTMENTS—The Registrar, The University, Liverpool (August 23).

SENIOR LECTURER or LECTURER IN THE DEPARTMENT OF PHILOSOPHY with special qualifications in Political Philosophy—The Registrar, The University, Manchester 13 (August 23).

DEPUTY CITY ANALYST—The Town Clerk, City Council Chambers, 1 Clarence Parade, Southsea, Hants (August 30).

LABORATORY ASSISTANT at the Marine Biological Station, Millport—The Secretary, Scottish Marine Biological Association, 185 St. Vincent Street, Glasgow, C.2 (August 30).

LECTURER IN CHEMISTRY (Inorganic and Analytical Chemistry) in University College, Dundee—The Secretary, The University, St. Andrews (August 30).

ASSISTANT ANALYST—The City Analyst, 152 Great Charles Street, Birmingham 3 (August 30).

SENIOR LECTURER IN BOTANY in the Rhodes University College, Grahamstown—The Secretary, Office of the High Commissioner for the Union of South Africa, Trafalgar Square, London, W.C.2 (August 31).

LECTURER IN BIOCHEMISTRY—The Professor of Chemical Pathology, British Postgraduate Medical School, Ducane Road, London, W.12 (September 1).

ASSISTANT (Lecturer) IN THE DEPARTMENT OF BIOLOGY—The Secretary, Medical School, Middlesex Hospital, London, W.1 (September 1).

READERSHIP IN ECONOMICS (Banking and Currency) tenable at the London School of Economics—The Academic Registrar, University of London, Senate House, London, W.C.1 (September 4).

SENIOR EXPERIMENTAL OFFICER or EXPERIMENTAL OFFICER (temporary), Atomic Energy Research Establishment, Harwell, Didcot, Berks—The Ministry of Labour and National Service, Technical and Scientific Register, Room 171, York House, Kingsway, London, W.C.2, quoting A.261/47A (September 5).

PRINCIPAL SCIENTIFIC OFFICER or SENIOR SCIENTIFIC OFFICER (temporary), Atomic Energy Research Establishment, Harwell, Didcot, Berks—The Ministry of Labour and National Service, Technical and Scientific Register, Room 171, York House, Kingsway, London, W.C.2, quoting A.260/47A (September 5).

SENIOR SCIENTIFIC OFFICER or SCIENTIFIC OFFICER (temporary), Atomic Energy Research Establishment, Harwell, Didcot, Berks—The Ministry of Labour and National Service, Technical and Scientific Register, Room 171, York House, Kingsway, London, W.C.2, quoting A.259/47A (September 5).

PRINCIPAL SCIENTIFIC OFFICER (temporary), Atomic Energy Research Establishment, Harwell, Didcot, Berks—The Ministry of Labour and National Service, Technical and Scientific Register, Room 171, York House, Kingsway, London, W.C.2, quoting A.258/47A (September 5).

DEPUTY TO THE CITY ANALYST—The Medical Officer of Health, Public Health Department, Leeds, endorsed 'Deputy City Analyst' (September 8).

ENGINEER CONTROL OFFICERS (temporary), Atomic Energy Research Establishment, Harwell, Didcot, Berks—The Ministry of Labour and National Service, Technical and Scientific Register, Room 171, York House, Kingsway, London, W.C.2, quoting C.417/47A (September 13).

LECTURERS (2) IN MATHEMATICS—The Secretary, King's College, Strand, London, W.C.2 (September 15).

LECTURER (ungraded) IN VETERINARY PARASITOLOGY, and a LECTURER (Grade II) IN MARINE BIOLOGY at the Port Erin Station—The Registrar, The University, Liverpool (September 15).

PROFESSOR OF CHEMISTRY in University College, Dundee—The Secretary, The University, St. Andrews (September 15).

RECTOR OF CANTERBURY UNIVERSITY COLLEGE, Christchurch, New Zealand—The Secretary, Universities Bureau of the British Empire, 8 Park Street, London, W.1 (September 15).

READER IN ANTHROPOLOGY in the Department of Geography in the Newcastle Division of the University—The Registrar, University Office, 46 North Bailey, Durham (September 15).

CHAIR OF COMPARATIVE PHILOLOGY OF SLAVONIC LANGUAGES tenable at the School of Slavonic and East European Studies—The Academic Registrar, University of London, Senate House, London, W.C.1 (September 23).

SOIL CHEMIST IN THE DEPARTMENT OF AGRICULTURE AND FORESTS, Sudan Government Research Division—The Sudan Agent, Wellington House, Buckingham Gate, London, S.W.1, endorsed 'Soil Chemist' (September 30).

CHAIR OF TOWN AND COUNTRY PLANNING in the University of Sydney—The Secretary, Universities Bureau of the British Empire, 8 Park Street, London, W.1 (Sydney, September 30).

ECONOMIC ENTOMOLOGIST and an ENTOMOLOGIST for research (particularly on control) and general survey of all insect life of the country, and an ENTOMOLOGIST for work in the Plant Protection Division on general applied entomology and pest control (not research), to the Directorate-General of Agriculture, Government of Iraq—The Crown Agents for the Colonies, 4 Millbank, London, S.W.1, quoting M.N.12711.

HEAD OF THE BUILDING AND CIVIL ENGINEERING DEPARTMENT—The Acting Principal, Royal Technical College, Salford 5.

SENIOR LECTURER IN PHYSICS—The Clerk, Northern Polytechnic, Holloway, London, N.7.

ASSISTANT RESEARCH CHEMISTS (2) in the Hop Research Department—The Registrar, Wye College, Wye, Ashford, Kent.

LECTURER IN PHYSICS—The Registrar, The University, Reading.

LECTURER IN ELECTRICAL ENGINEERING, a LECTURER IN MECHANICAL ENGINEERING, a LECTURER IN CIVIL or STRUCTURAL ENGINEERING, a LECTURER IN PRODUCTION ENGINEERING, and a LECTURER IN AUTOMOBILE ENGINEERING, in the Chance Technical College—The Chief Education Officer, 215 High Street, Smethwick 41.

QUALIFIED PHYSICIST or ENGINEER with mathematical ability to join a research team investigating rolling mill problems—The Personnel Officer, British Iron and Steel Research Association, 11 Park Lane, London, W.1, quoting 'Rolling Mill'.

RESEARCH ASSISTANT in the field of Organic Chemistry—The Secretary, King's College of Household and Social Science, Campden Hill Road, London, W.8.

LABORATORY TECHNICIANS (2, Grade B)—The House Governor, St. Mary's Hospital, Paddington, London, W.2.

RESEARCH ASSISTANTS (2, one with medical qualification or degree in a biological subject, the other with honours degree in organic chemistry)—The Secretary, Department of Chemotherapy, School of Tropical Medicine, Pembroke Place, Liverpool 3.

FORESTER as Head of a Forestry Division for the Directorate General of Agriculture, Government of Iraq, The Crown Agents for the Colonies, 4 Millbank, London, S.W.1, quoting M.N.18183.

LABORATORY TECHNICIAN (male)—The Secretary, Department of Parasitology, School of Tropical Medicine, Pembroke Place, Liverpool 3.

ASSISTANT LECTURER IN PHYSICS—The Registrar, University College, Exeter.

SENIOR LECTURER or LECTURER IN PHILOSOPHICAL PSYCHOLOGY, and an ASSISTANT LECTURER IN EXPERIMENTAL PSYCHOLOGY, in the University of Otago, Dunedin—The High Commissioner for New Zealand, 415 Strand, London, W.C.2.

HYDROGRAPHICAL SURVEYOR (Grade III) by the Government of Iraq for the Basrah Port Directorate—The Crown Agents for the Colonies, 4 Millbank, London, S.W.1, quoting M.N.17048.

CURATORSHIP OF THE ZANZIBAR PEACE MEMORIAL MUSEUM—The Director of Recruitment, Colonial Service, 15 Victoria Street, London, S.W.1.

LECTURER IN ELECTRICAL ENGINEERING, Technical Institute, Lagos, Nigeria—The Director of Recruitment, Colonial Service, 15 Victoria Street, London, S.W.1.

HOOD PROFESSOR OF MINING—The Secretary, The University, Edinburgh.

DIRECTOR OF MUSEUMS, Museums Department, Malaya, and a CURATOR of the Perak Museum, at Taiping—The Director of Recruitment, Colonial Service, 15 Victoria Street, London, S.W.1.

LECTURER IN HORTICULTURE in relation to commercial glasshouse production—The Director, School of Agriculture, Sutton Bonington, Loughborough.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences. No. 589, Vol. 232: Experimental Investigations of the Shoot Apex of *Dryopteris aristata* Druce. By C. W. Wardlaw. Pp. 343–384 + plates 10–14. (London: Cambridge University Press, 1947.) [6d]

Collective Index of the Journal of the Institute of Brewing, 1935 to 1945. Compiled by W. H. Bird and Pamela Moore Bell. Pp. iv + 210. (London: Institute of Brewing, 1946.) [6s]

Royal Society Empire Scientific Conference, June–July 1946. Preliminary Report. Pp. 68. (London: Royal Society, 1947.) [6s]

Other Countries

Simon Velikovsky Foundation. Scientific Report 4: Cosmos without Gravitation: Attraction, Repulsion and Electromagnetic Circumduction in the Solar System. Synopsis by Immanuel Velikovsky. Pp. iv + 24. (New York and Tel-Aviv: Simon Velikovsky Foundation, 1946.) [6s]

Papers in Physical Oceanography and Meteorology. Vol. 9, No. 4: A Study of Interdiurnal Pressure and Temperature Variations in the Free Atmosphere over North America. By Thomas F. Malone. Pp. 50. (Cambridge, Mass.: Massachusetts Institute of Technology, 1946.) 75 cents. [6s]

Meddelanden från Oceanografiska Institutet i Göteborg. 10: Photometric Measurements of the Growth of Phytoplankton Cultures. By F. Gross and F. F. Koczy. Pp. 18. 11: The Photosynthetical Effect of Ultra-violet Radiation on some Marine Algae. By N. G. Johnson and T. Levring. Pp. 5. (Göteborg: Elanders Boctrycker A.-B., 1946.) [6s]